



# THE JOURNAL OF GENERAL PHYSIOLOGY

*Founded by Jacques Loeb*

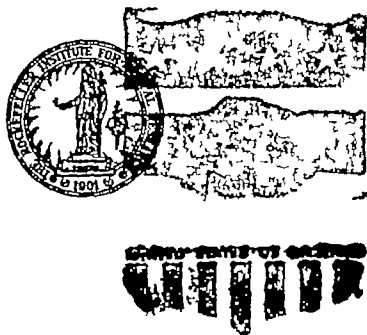
W J CROZIER

JOHN H NORTHROP

W J V OSTERHOUT

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EDITORS

W J CROZIER

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## CONTENTS

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CROZIER, W J, and WOLF, ERNST Theory and measurement of visual mechanisms VI On flicker with subdivided fields	40
SOLLNER, KARL, and ANDERMAN, JOAN The structure of the collodion membrane and its electrical behavior VIII Quantitative studies concerning the acidic properties of collodion and their correlation with membrane structure and activity	43
SOLLNER, KARL, and BECK, PAUL W The structure of the collodion membrane and its electrical behavior IX Water uptake and swelling of collodion membranes in aqueous solutions of organic electrolytes and non-electrolytes	451
ORMSBEE, RICHARD A, and FISHER, KENNETH C The effect of urethane on the consumption of oxygen and the rate of cell division in the ciliate <i>Tetrahymena geleii</i>	461
FISHER, KENNETH C, and HENRY, R J The effects of urethane and chloral hydrate on oxygen consumption and cell division in the egg of the sea urchin, <i>Arbacia punctulata</i>	469

---

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## CONTENTS

---

PONDER, ERIC    The kinetics of <i>in vivo</i> hemolytic systems	483
CROZIER, W J, and WOLF, ERNST    Theory and measurement of visual mechanisms    XII    On visual duplexity	513
GOLDSTEIN, AVRAM.    The mechanism of enzyme-inhibitor substrate reactions illustrated by the cholinesterase-physostigmine-acetylcholine system	529
INDEX TO VOLUME 27	581

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# THEORY AND MEASUREMENT OF VISUAL MECHANISMS

## XI. ON FLICKER WITH SUBDIVIDED FIELDS

By W J CROZIER AND ERNST WOLF

(From the Biological Laboratories, Harvard University, Cambridge)

(Received for publication, December 17, 1943)

### I

When visual flicker is produced by passing vertical dark bars across an illuminated field<sup>1</sup> with fixed inclined opaque stripes on it, certain pronounced changes are induced in the properties of the flicker contour<sup>2, 3</sup>.

Ordinarily, with image fields not subdivided, and regardless of whether flicker is produced by sectoring the light beam at a focus<sup>4</sup> or by the striped cylinder technic, the dependence of the contour for flicker recognition on the light time fraction  $t_L$  in the flash cycle is direct and simple.<sup>5</sup> The maximum flash frequency  $F$  to which the  $F - \log I$  curve asymptotically rises declines rectilinearly with increase of  $t_L$ , its abscissa of inflection (photopic "cone" segment) increases rectilinearly with  $t_L$ , and the third parameter of the probability summation<sup>6</sup> describing the simplex  $F - \log I$  curve, namely the standard deviation  $\sigma'_{\log I}$  of its first derivative in  $\log I$  with  $F_{\max}$  put = 100, is found not to change at all when  $t_L$  is altered. (In certain cases, with most arthropods,<sup>7</sup> slight changes in the shape of the lower part of the curve arise as a consequence of the convexity of the surface of the eye but this does not affect the essential generality of the previous statement.) Fundamentally the behavior of the scotopic "rod" part of duplex  $F - \log I$  contours is the same, but this may be obscured by the integrated overlapping of the "rod" and "cone" populations of neural effects.<sup>8</sup>

With an obliquely barred field however and flicker produced by evenly

<sup>1</sup> Wolf, E. and Zerrahn Wolf G. 1935-36 *J Gen Physiol*, 19, 495. Crozier, W. J., Wolf, E., and Zerrahn Wolf G. 1936-37 *J Gen Physiol*, 20, 211, 1937-38, 21, 203, etc.

<sup>2</sup> 1941-42 *J Gen Physiol*, 25, 369.

<sup>3</sup> 1943-44, *J Gen Physiol*, 27, 287.

<sup>4</sup> 1940-41 *J Gen Physiol* 24, 505, 635, 1941-42, 25, 89, 293, 1943-44, 27, 119.

<sup>5</sup> 1937-38 *J Gen Physiol* 21, 313, 463. *Proc. Nat. Acad. Sc.*, 1940, 26, 60, *J Gen Physiol* 1939-40 23, 531.

<sup>6</sup> 1938-39, *J Gen. Physiol.* 22, 311, 451, 1940-41, 24, 625, 1941-42, 25, 369, 1943-44, 27, 119.

<sup>7</sup> 1937-38, *J Gen Physiol* 21, 463.

<sup>8</sup> 1937-38, *J Gen Physiol*, 21, 313, 1940-41, 24, 635.

spaced vertical bars moving across it, the shape constant  $\sigma'_{\log I}$  is sharply decreased above  $t_L = 0.50$ , so that the contour is then much steeper,  $\tau'$  does not increase as much as with a plain field, and neither  $\tau'$  nor  $F_{max}$  is a simple function of  $t_L$ . These effects cause the curves for large values of  $t_L$  to cut across those for the smaller values, instead of being evenly and symmetrically spaced as with the plain field.

This latter picture is the one obtained for the sets of  $F - \log I$  contours at different values of  $t_L$  secured with birds,<sup>9</sup> by the revolving stripe method. The birds used possess large, well developed pectens. The theory<sup>3</sup> is that the moving contact of bar images with the serrated shadow of the pecten causes the natural occurrence of the phenomenon experimentally induced in man by the use of the obliquely barred field.

Partly as a test of this conception, partly for other reasons, we have examined the results to be obtained when transilluminated parts of stationary barred patterns of different sorts are caused to flicker simultaneously by sectoring the light at a focus. The point then is that, a standing pattern being intermittently illuminated, one can inquire whether subdivision of the flickered field into several parts will of itself introduce modification of the properties of the set of flicker contours when  $t_L$  is varied, and whether such modification will be similar to that involved in the "pecten effect". From another standpoint, it is to be noted that we can also examine by this means the problem of neural integration in visual excitation.<sup>10</sup> The relation between  $F$  and  $\log I$  critical for flicker, although simultaneously apparent in the several parts of a subdivided field, is not the same as when one of its parts is tested separately or when a simple field of the same general form and the same total illuminated area is flickered.

We are more immediately concerned with the demonstration that the "pecten effect" is only in part reproduced in the changes actually effected in the properties of the  $F - \log I$  contour by the "stationary flickering" of subdivided fields. The character of the changes found substantiates the importance of the "sliding contact" of stationary and moving dark images for the production of enhanced flicker acuity by the "pecten effect".

The results here given also extend the basis for an understanding of the manner in which "rod" and "cone" effects are integrated to produce the  $F - \log I$  contour in the region of their overlapping. They likewise bear directly upon the curious properties of "visual acuity" with interrupted light, which we discuss in a following paper. And, in a more general connection, the data here cited complete the proof that three independently modifiable parameters ( $F_{max}$ ,  $\tau'$ ,  $\sigma'_{\log I}$ ) are involved in the nature of the flicker contour.

<sup>9</sup> 1943-44, *J. Gen. Physiol.*, 27, 315

<sup>10</sup> Cf. 1940-41, *J. Gen. Physiol.*, 24, 505, 1941-42, 25, 369, and a following paper

## II

The general procedure followed in these experiments, the instrumentation, and the methods of calculation, have been described previously.<sup>11</sup> The four fields used for the present discussion are (i) a square subtending at the retina  $3^\circ$  on a side, centered  $6^\circ$  horizontally on the temporal aspect of the left retina (ii) a square subtending  $3^\circ$  on a side, with horizontal and vertical subdivision into four equal squares (Fig. 1) the opaque dividing stripes being  $0.3^\circ$  broad, centered as for (i) The crossed bars were formed of pieces of wristwatch hair-spring mounted in the jaws of the spectroscopic slit in one arm of our discriminometer.<sup>12</sup> The total illuminated area with (i) and (ii) was taken to be nearly enough the same, despite scattered light on the crossbars (iii) A square subtending  $10^\circ$  on a side, centered at the fovea, with three opaque vertical bars each  $1.43^\circ$  wide thus giving four vertical illuminated spaces of that width equally separated, and (iv) a square  $10^\circ$  (really  $9.91^\circ$ ) on a side with six opaque vertical bars and seven illuminated bars all of  $0.77^\circ$  width. Thus the bars in (iv) were of about one-half the width of those in (iii) and the total illuminated area in (iv) was a little less (52.9 square degrees as compared with 57.2 square degrees). For certain tests field (iv) was rotated  $90^\circ$  so that the stripes were horizontal we may speak of this as field (v). The opaque bars were produced by hard photographic reduction of carefully made contact prints of Levy plates mounted in the spectroscopic slits of the discriminometer.

The observations were made monocularly (left eye). Tungsten white light was used with (ii) and the white and a red and a blue filtered from it with the other fields.

## III

The data for fields (i) and (ii) are given in Tables I and II. In Figs. 1 and 2 it is seen that the nature of the shift in contours with change of light time fraction  $t_L$  is of the kind already found for plain fields.<sup>11</sup> In the subdivided field (ii) there is no change of the slope constant at  $t_L = 0.90$  nor any change in the type of relation of  $\tau'$  to  $t_L$  and in this sense there is no pronounced 'pecten effect'.<sup>13</sup> But the picture is nevertheless changed considerably when the  $3^\circ$  square is subdivided into four parts. The 'rod' segment is then greatly enlarged, the 'cone' segment becomes much steeper and its midpoint is moved to a higher flash intensity. The interrelation of these two phenomena we shall consider shortly. The slight increase in over-all illuminated area in (ii), by scattered light on the crossbar images, cannot possibly account for them.<sup>12</sup> The steepening of the 'cone' segment is a prominent feature of the "pecten effect," but when this effect occurs it is seen only with longer light times in the flash cycle,<sup>2</sup> here it is independent of  $t_L$ . It is perfectly clear, as already emphasized elsewhere,<sup>10</sup> that pronounced changes of the shape constants of the flicker contours make futile any attempt to deduce from such constants alone

<sup>11</sup> 1940-41, *J. Gen. Physiol.* 24, 505-635 1941-42, 25-89 293

<sup>12</sup> 1938-39 *J. Gen. Physiol.* 22 341

<sup>13</sup> Cf. following paper



TABLE I

Data for flicker recognition contours with a  $3^\circ$  square image centered  $6^\circ$  on the temporal side of the fovea (W J C, monocular observations with *left* eye), white light, flash intensities  $I$  in millilamberts, " $t_L$ " =  $t_L/(t_L + t_D)$ ,  $n = 10$  for each point

$F$ per sec	$t_L = 0.10$ $\log I_m \quad \log P E_1$	$t_L = 0.50$ $\log I_m \quad \log P E_1$	$t_L = 0.90$ $\log I_m \quad \log P E_1$
2		$\bar{6}$ 6095 $\bar{7}$ 0405	$\bar{5}$ 0686 $\bar{7}$ 5487
4		$\bar{6}$ 6736 $\bar{7}$ 1897	$\bar{5}$ 0723 $\bar{7}$ 5454
5		$\bar{6}$ 9373 $\bar{7}$ 7479	$\bar{5}$ 4216 $\bar{7}$ 8757
7		$\bar{6}$ 9346 $\bar{7}$ 3341	$\bar{5}$ 5516 $\bar{6}$ 1567
8	$\bar{6}$ 3649 $\bar{8}$ 8924	$\bar{5}$ 2384 $\bar{6}$ 5384	$\bar{5}$ 5456 $\bar{6}$ 0957
9			$\bar{5}$ 8187 $\bar{6}$ 4270
10	$\bar{6}$ 6949 $\bar{7}$ 1411	$\bar{5}$ 5753 $\bar{6}$ 1377	$\bar{5}$ 9594 $\bar{6}$ 4233
12	$\bar{5}$ 0962 $\bar{7}$ 5690	$\bar{5}$ 9848 $\bar{6}$ 4544	$\bar{5}$ 9996 $\bar{6}$ 3734
15	$\bar{5}$ 7021 $\bar{6}$ 1747	$\bar{4}$ 5838 $\bar{5}$ 0917	$\bar{4}$ 2148 $\bar{6}$ 6676
18	$\bar{4}$ 4195 $\bar{6}$ 9416	$\bar{3}$ 2765 $\bar{5}$ 7621	$\bar{4}$ 4717 $\bar{5}$ 1499
20	$\bar{4}$ 7667 $\bar{5}$ 2744	$\bar{3}$ 6166 $\bar{5}$ 9389	$\bar{4}$ 4758 $\bar{6}$ 8742
22	$\bar{4}$ 9610 $\bar{5}$ 3297	$\bar{3}$ 8228 $\bar{4}$ 2854	$\bar{4}$ 9366 $\bar{5}$ 5446
25	$\bar{3}$ 2548 $\bar{5}$ 8353	$\bar{2}$ 1268 $\bar{4}$ 5204	$\bar{4}$ 9349 $\bar{5}$ 4200
30	$\bar{3}$ 7843 $\bar{4}$ 2037 $\bar{3}$ 7913 $\bar{4}$ 2042	$\bar{2}$ 6770 $\bar{3}$ 1989	$\bar{3}$ 4493 $\bar{4}$ 1306
33		$\bar{2}$ 9478 $\bar{3}$ 3516	$\bar{3}$ 4767 $\bar{4}$ 0262
35	$\bar{2}$ 2567 $\bar{4}$ 7288	$\bar{1}$ 0934 $\bar{3}$ 6108	$\bar{2}$ 1467 $\bar{4}$ 6338
38		$\bar{1}$ 4495 $\bar{2}$ 0345	$\bar{2}$ 1235 $\bar{4}$ 5924
40	$\bar{2}$ 8010 $\bar{3}$ 4135	$\bar{1}$ 6660 $\bar{2}$ 1924	$\bar{2}$ 4818 $\bar{4}$ 9490
43		0 0697 $\bar{2}$ 5342	$\bar{2}$ 4929 $\bar{4}$ 9477
45	$\bar{1}$ 5326 $\bar{3}$ 9451	0 4681 $\bar{2}$ 8685	$\bar{2}$ 4729 $\bar{4}$ 9179
47		0 6931 $\bar{1}$ 1354	$\bar{2}$ 7069 $\bar{3}$ 2570
48	0 2858 $\bar{2}$ 6592	1 2014 $\bar{1}$ 7156	$\bar{2}$ 7207 $\bar{3}$ 2527
49			$\bar{2}$ 9932 $\bar{3}$ 4692
50		2 3454    0 8464	$\bar{1}$ 0022 $\bar{3}$ 4720
51	1 5486 $\bar{1}$ 8261	2 3420    0 9756	$\bar{1}$ 3801 $\bar{3}$ 8726
52		3 4087    1 0384	$\bar{1}$ 3860 $\bar{3}$ 8497
			$\bar{1}$ 7179 $\bar{2}$ 2809
			$\bar{1}$ 8988 $\bar{2}$ 2872
			$\bar{1}$ 9057 $\bar{2}$ 3942
			0 2808 $\bar{2}$ 8894
			0 5603 $\bar{1}$ 0728
			0 5470 $\bar{2}$ 9529
			0 9619 $\bar{1}$ 5318
			1 3294 $\bar{1}$ 9665
			1 3440 $\bar{1}$ 8679
			1 8013    0 2591
			2 1970    0 9468
			2 2201    0 6583
			3 0287    1 4591
			2 9605    1 4342
			2 9843    1 4817

clues as to the physicochemical character of the primary excitation process. Mere subdivision of the illuminated area could not possibly change "reaction

TABLE II

Data for flicker contours obtained with a square image area totaling 9 square degrees, subdivided into four equal squares by vertical and horizontal cross-bars each 0.3 wide the center of the cross being 6° on the temporal side of the fovea. These data are to be compared with those in Table I for the simple 3 × 3 square all in one piece. Observer W J C left eye  $n = 10$

$F$ per sec	$t_L = 0.10$		$0.50$		$0.90$	
	$\log I_m$	$\log P.E.$	$\log I_m$	$\log P.E.$	$\log I_m$	$\log P.E.$
2	5 5296	6 0437	4 0358	6 5216	4 5362	5 0705
6	5 8706	6 1621	4 5635	6 7251	4 8958	5 3624
10	4 1544	6 5098	4 6482	6 9960	5 1878	5 6541
14	4 5781	5 1187	5 0715	5 5204	5 6383	5 9576
16					5 8078	4 2777
17	4 8337	5 5105				
18			5 8185	4 0338	5 1664	4 4564
19	5 4663	5 9983	5 0496	4 4241	5 5256	4 9719
20	5 7858	4 1610	5 5806	4 9877	5 3895	5 7798
	5 7833	4 1414	5 5841	4 9999	5 4338	2 0034
22	5 4901	4 9249	5 0638	5 5854	5 6647	2 1363
	5 4384	4 8552	5 1018	5 5762	5 6244	2 0608
25	5 9091	5 4289	5 4815	5 9960	5 8952	2 3080
			1 3236	5 7931		
			5 4112	5 7547		
30	5 2251	5 6523	5 8242	2 1775	0 1718	2 6365
			5 6678	2 0844		
			5 6813	2 0173		
35	5 5678	5 9732	5 9635	2 1273	0 4717	2 8669
			0 0146	2 5026		
40	1 8965	2 3267	0 3837	2 7324	0 8237	1 2419
			0 3683	2 7843		
45	0 4712	2 8844	1 0062	1 6089	1 4786	1 8508
			0 9528	1 3601		
48	0 9999	1 5367	1 3676	1 6347	2 0481	0 4123
			1 5210	1 8894		
			1 5217	0 0420		
50	1 5181	1 9547	2 1603	0 7309	2 7521	1 3171
			1 9760	0 4015		
51	2 6747	1 1632	2 6747	1 1632		
			3 0448	1 5308		

orders." Table II includes at  $t_L = 0.90$  two sets of measurements made about a year apart. They show good agreement.

In correlation with the abrupt steepness of the photopic curves in Fig 2, we note that  $F_{max}$  does not change so rapidly with  $t_L$  (Fig 3 b), although the rate

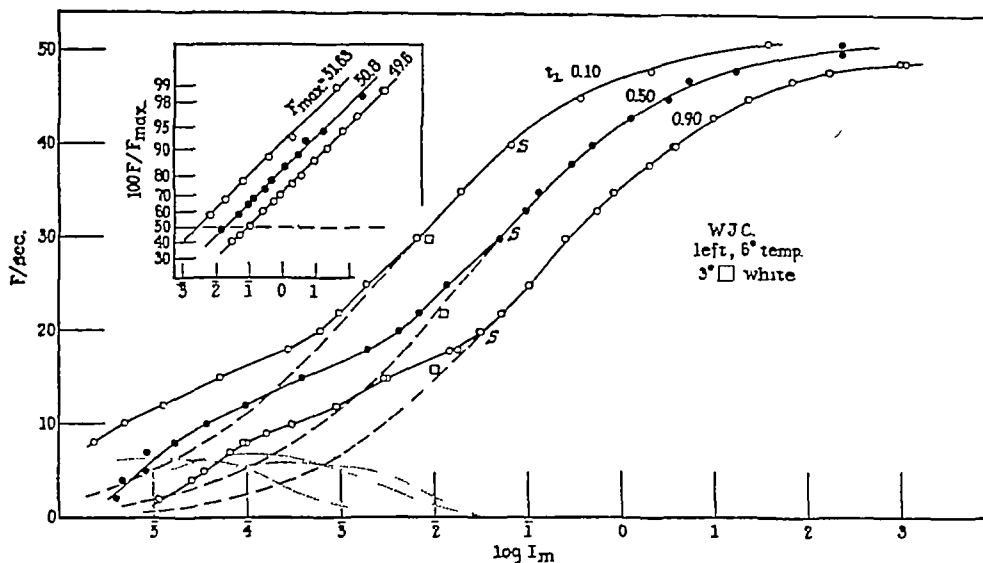


FIG 1  $F - \log I$  contours for a  $3^\circ$  square image, centered  $6^\circ$  horizontally on the temporal side of the left fovea, white light, light-time fractions  $t_L = 0.10, 0.50, 0.90$ . The inset figure shows the upper portions of these curves on a probability grid, computed to the values of  $F_{max}$  indicated, to show that the slope constants ( $\sigma'_{\log I}$ ) are identical. These probability integrals are shown extrapolated, below, and the separated "rod" contributions are given by the dotted lines. Data in Table I.

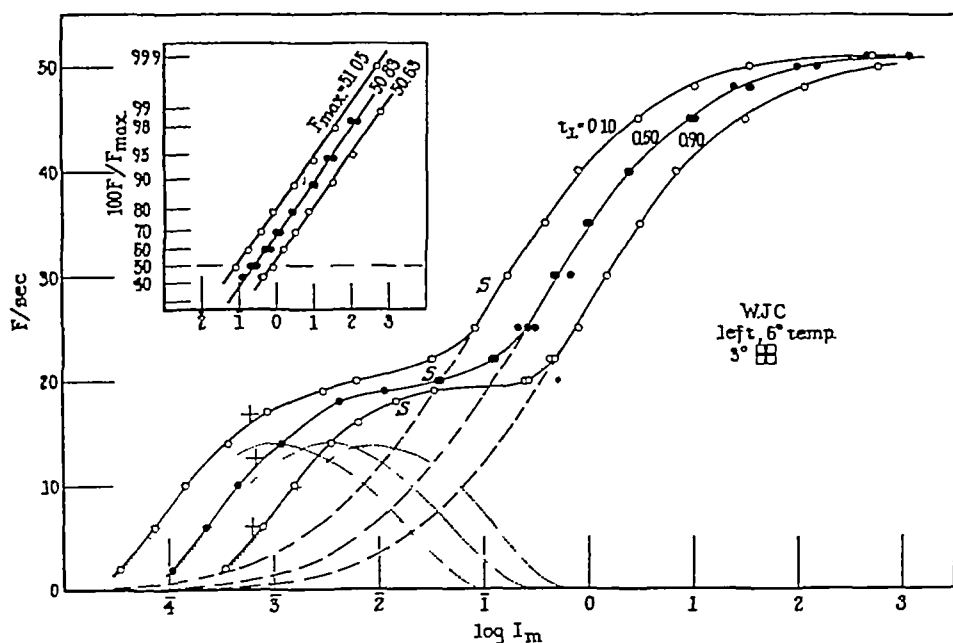


FIG 2 Conditions as in Fig 1, but here the  $3^\circ$  square has been subdivided into four equal parts, separated by dark bars  $0.3^\circ$  broad (see text). Data in Table II. In comparison to the curves in Fig 1,  $\sigma'_{\log I}$  is less, but is again the same for the three values of  $t_L$ . The scotopic segments are much larger than in Fig 1. The ascending and the descending branches of the separated-out "rod" components are probability integrals drawn with  $F_{max} = 14.25, 14.25, 13.9$ .

of change of the abscissa of inflection  $\tau'$  (Fig. 3a) is about the same as for the undivided field of the same total illuminated area.

In general, above a certain small size, increase of image area  $A$  in a given retinal region causes the "cone" curve to become steeper.<sup>13</sup> Comparisons with contours for image sizes larger and smaller than  $3^\circ \times 3^\circ$ , centered at  $6^\circ$  from the fovea, show that the slope increases with  $A$  in this way.<sup>13</sup> The interpretation that this is due to the involvement of a larger number of cone units is consistent with the facts that the slope constant  $\sigma'_{\log I}$  is (a) independent of  $t_L$  and of temperature<sup>14</sup> although a function of wave length, and (b) it changes in the expected way when a given illuminated patch is placed at different locations on the retina where the numbers of cone units differ. The evidence is consid-

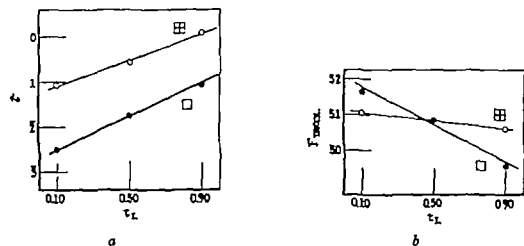


FIG. 3. The rectilinear relations of  $\tau'$  to  $t_L$  and of  $F_{max}$  to  $t_L$  are shown for the (photopic)  $F - \log I$  contours of Figs. 1 and 2.

ered in some detail in a following paper.<sup>15</sup> The argument for the necessity of dealing with all the available units at all levels of  $F$  and  $I$  has been set out previously.<sup>14</sup>

The question arises whether this can be the explanation for the difference between the "cone" slope constants in Figs. 1 and 2. We believe that it can. The flicker end point is conceived to be brought about, neurally, by the production of a certain frequency of what we have termed "elements of effect," the same end point, namely recognition of flicker, can be achieved by a smaller average number of such elements from each of a larger number of neural units or by a greater mean contribution from each of a smaller number of units. Subjectively at the end-point all of the illuminated field, subdivided or not, is seen to flicker at once, but the effect is sharper at the boundaries. It is important to realize that the modification of the flicker contours with field (ii)

<sup>13</sup> 1937-38 *J. Gen. Physiol.* **21**, 313; 1938-39 **22**, 311; 1939-40 **23**, 531; 1940-41 **24**, 635; 1941-42 **25**, 89; 293; 369; 1943-44 **27**, 119.

<sup>15</sup> 1943-44 *J. Gen. Physiol.* **27**, 119.

appears well below the brightness level at which there is perception of the fact that the field is actually subdivided (*e g*, with  $t_L = 0.10$ , the bars are not visible until a flash intensity of  $4.80 \log \text{ ml}$  units is reached). In comparison to the  $3^\circ$  square field, the square broken into four parts has twice the perimeter of light/dark separation. The  $F - \log I$  contours can be compared with those for a  $6^\circ$  square, having very nearly the same perimeter as that of field (u). The comparison is not altogether simple, since the shifts of  $\tau'$  with  $t_L$  are not the

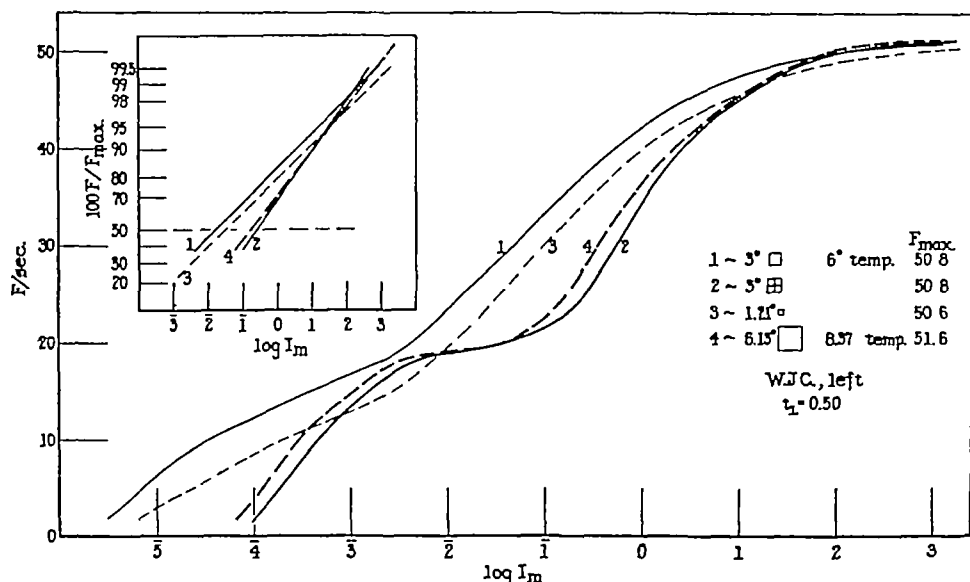


FIG. 4. Certain  $F - \log I$  contours,  $t_L = 0.50$ , for square images (white light), centered at *ca*  $6^\circ$  on the temporal side of the left fovea (W. J. C.), are traced for comparison. See text. The heavier continuous line for the  $3^\circ$  square area subdivided into four equal parts approaches quite near to the heavier dashed line for the simple  $6.13^\circ$  square (centered  $8.4^\circ$  off the fovea, there is no real difference produced, for such a square, by the slightly more temporal centering, which, however, has for our purpose certain advantages).

The inset graphs show the upper parts of the main contours on a probability grid. See text.

same, but qualitatively the indications are suggestive (Fig. 4). Here we have traced the curves for several image areas at  $t_L = 0.50$ . The contours for the  $6^\circ$  and the subdivided  $3^\circ$  squares are even closer together at  $t_L = 0.90$ ,  $t_L = 0.50$  was chosen because there the several values of  $F_{max}$  are closest together. Fig. 4 shows that one of the four parts of field (u) gives a curve very little changed from that for the simple  $3^\circ$  square (i), but that doubling the extent of the light/dark edge, keeping  $A$  constant, has about the same effect as doubling the size of the square. The conception of a smaller mean contribution with (u)

from each excitable unit, that is a smaller frequency of elements of effect from each, is strengthened by the greatly reduced change of  $F_{max}$  with change of  $t_L$ .

This general conclusion as to the significance of the lines of light-dark separation is reinforced by the findings in the experiments of section V. It has already been stressed in another connection, namely in the data on the excitation of the eyes of bees,<sup>19</sup> but there it is primarily a matter of the total frequency with which impulses are being generated, and the eye area illuminated at any instant is not the same when more stripes are introduced into a field. On the other hand, when checker board fields are used, with  $I$  the same, fields with the same black-white perimeter have the same excitatory value for the bee although  $A$  is quite different.

The significance of contours in the flickered field, of course introduces a somewhat novel factor into the interpretation of tests made in search of evidence for "summation" and the like by placing one flickered patch near to another one. The most important feature of the situation may then be, not that the total illuminated area has been increased, but that there is an unilluminated zone between the patches. This is not to say that the image area is not a significant factor, however. The interesting points arising in relation to the rôle of the form of the image and of the differential illumination of its several parts, we cannot now discuss. One approach to the question of the relative rôles played by total illuminated area on the one hand and on the other by image contour, is undertaken in section V.

The dynamical interrelations of the groups of "rod" and "cone" effects in critical flicker have been discussed<sup>20</sup> in terms of the partial inhibition of rod units by the activation of cone units, and the statistical summation in terms of probability integrals of the remainder with the cone effects. It follows from this conception that if the cone curve can be made steep enough, and moved to relatively higher intensities, the rising branch of the scotopic  $F - \log I$  curve could be completely freed from cone involvement.<sup>10</sup> This we have found to occur normally in certain fishes.<sup>17</sup> The effect has been produced in the human  $F - \log I$  contour by imposition of several kinds of special conditions,<sup>18</sup> but ordinarily the rod contribution must be extracted by subtraction of ordinates of the extrapolated "cone curve."<sup>19</sup> The present data on fields (i) and (ii) illustrate and justify these principles. It is apparent (Figs 1 and 2) that with the subdivided field the scotopic branch of the con

<sup>14</sup> Wolf E. 1932-33 *J. Gen. Physiol.* 16, 773. Wolf E. and Crozier W. J. 1932-33 *J. Gen. Physiol.* 16, 787. Zerrahn G. 1933 *Z. Vergleich. Physiol.* 20, 117, 151. Wolf E. and Zerrahn G. 1934-35 *J. Gen. Physiol.* 18, 853.

<sup>17</sup> 1937-38, *J. Gen. Physiol.*, 21, 17. *Proc. Nat. Acad. Sc.*, 1937, 23, 516. *J. Gen. Physiol.* 1938-39, 22, 463.

<sup>18</sup> 1941-42 *J. Gen. Physiol.* 25, 369. 1943-44, 27, 287.

<sup>19</sup> Cf. 1937-38 *J. Gen. Physiol.*, 21, 203, 313. 1940-41, 24, 505. 1941-42, 25, 369.

tour is greatly enlarged, although it falls at higher intensities. The analysis<sup>19</sup> shown indicates that when the lower tail of the "cone" curve is caused to slip out from under the "rod" curve the latter increases in ordinate size, as expected. It cannot very well be supposed that the number of anatomical retinal rod units has been increased by the mere putting of crossbars on the field, or that their intensity thresholds have been profoundly increased thereby.

There are two general routes of escape from analytical difficulties created in such connections. One may suppose that the data are of neural origin, in the retina, central to the layer of primary receptors. Or it may be presumed that the quantitative properties of the data are of central nervous origin, even with

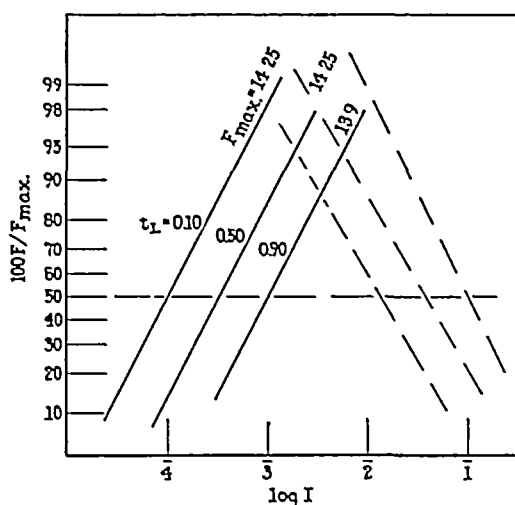


FIG. 5 The separated-out "rod" portions of the low intensity segments of the contours in Fig. 2, for the subdivided  $3^\circ$  square, shown on a probability grid. (The rising branches are not so steep, i.e.  $\sigma'_{\log I}$  is greater, in comparison to the corresponding features for the simple  $3^\circ$  square in Fig. 1, signifying for the divided area an actual increase in functional number of "rod" units.)

monocular regard. There are good reasons for adopting the latter view, but they do not directly concern us now. It has been pointed out that "rod" curve flicker data, not "cone" complicated, exhibit certain significant properties which show them to be organically similar in basis of origin to the "cone" data. Thus the "rod" and "cone" curves in any one kind of animal are quantitatively shifted to the same, specific, extent as a function of change of temperature,<sup>20</sup> and of change in  $t_L$ .<sup>21</sup> It is on these grounds quite impossible to assert that there is a different organic basis for the nature of "rod" effects on the one hand

<sup>20</sup> 1939, *Proc Nat Acad Sc*, 25, 78, 171, 1938-39, *J Gen Physiol*, 22, 487, 1939-40, 23, 143.

<sup>21</sup> 1937-38, *J Gen Physiol*, 21, 313, 1940-41, 24, 635.

and "cone" effects on the other as exhibited in the performance contours, or to suppose that different chemical mechanisms underly them.<sup>22</sup> This evidence is consistent with the requirements of the experimentally determined fact that the resolution of the overlapping "rod" and "cone" contributions has now been demonstrated on a simple uniform, statistical basis, under a variety of conditions, which would not be possible if the determination of the properties of the data did not occur in a common, simultaneous locus. The results of the analysis of the variation of critical intensities are in agreement with this position.

The dissected-out scotopic functional contributions to the  $F - \log I$  contours of Figs. 1 and 2 are shown on a probability grid in Fig. 5. It is clear that

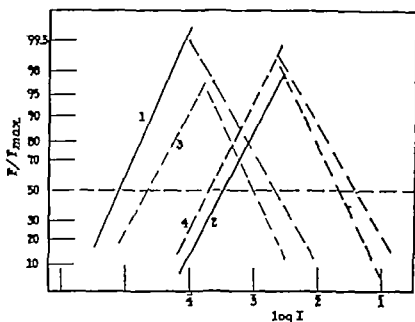


FIG. 6. Comparisons of the isolated "rod" components for the square images discussed in Fig. 4.  $t_L = 0.50$ .

the "rod"  $\tau'$  is again a rectilinear function of  $t_L$ , the proportionality constant is a little lower than for the "cone" branch,<sup>23</sup> and slightly lower than for the plain  $3^\circ$  square. From the comparisons in Fig. 4 it is apparent that the scotopic segment approaches that for the  $6^\circ$  square and the slope of the dissected-out "rod" curve does so likewise (Fig. 6).

#### IV

When flicker is produced by cutting a light beam at a focus, and repeated observations are made of the intensity  $I_c$  critical for flicker, it is found in all our series of measurements that  $\sigma_{11} \pm \sigma$  is in direct rectilinear proportion to  $I_c$  over the whole range of  $F$ , but that in general the proportionality factor and

<sup>22</sup> 1938 *Proc Natl Acad Sci*, **24**, 125; 1939, **25**, 171.

<sup>23</sup> Cf. 1940-41 *J Gen Physiol*, **24**, 635; 1941-42 **25**, 89, 293, etc.



$\sigma_\sigma$ , are not independent of  $A$ ,  $\lambda$ ,  $t_L$ , the observer, or the eye used. All this means that the mechanism producing the data is one in which a high degree of organically determined internal correlation prevails. Part of the correlation found is due to the use of the same instrument and a reasonably fixed procedure, of course. If necessary, this factor could be experimentally identified and arithmetically extracted. But under our conditions systematic changes of the indices of variation as brought about by altering  $t_L$ ,  $\lambda$ , or  $A$ , for example,<sup>24</sup> or the form of the image, or by using monocular *vs* binocular regard,<sup>25</sup> must be held to reflect properties of the observer in the system giving rise to the data.

The suggestion has been made<sup>26</sup> that in "absolute" threshold measurements, and so possibly in data on discriminations at higher levels of intensity, the real source of the variability encountered is in the stimulating light delivered rather than in the observer. This idea first arose in connection with data on threshold stimulation by single brief flashes,<sup>27</sup> where the possibility, if not indeed the significant actuality, of fluctuation in the number of quanta per single flash must be taken into account. The reality of any such consideration being required when trains of flashes are used (not shorter for the single flash than *ca* 0.009 second), with fairly large image areas, at high intensities, can be ruled out. Moreover the experimental fact is that (as we have repeatedly shown)  $\sigma_1/I_m$  is, for a given set of conditions, independent of intensity. But even for small, brief threshold flashes the argument proposed<sup>26</sup> is unacceptable. For this there are two reasons: the description of the dependence of responsiveness upon  $\Delta I_0$  by a Poisson summation<sup>26</sup> is not unequivocal, and if it could be shown to be unique, it could not be referred to discrete fluctuations in the "external" stimulus at the retina.

The point of the second reason is, that if integral (Poisson) variations of external light quantity occur, the mean total number of quanta being small, then in each of the media of the retina, and at each interface between media, random (Poisson) quantal losses will be suffered by the bundle of quanta in each flash, through absorption, reflection, and scattering. Now it is a fact inherent in the mathematical properties of such situations that successive superimposed Poisson effects cannot add up to produce a final Poisson distribution with respect to successive flashes. Gaussian distributions do add up in this way, and are the only ones which can.<sup>28</sup> Thus whether the frequency of positive threshold response is of Poisson form in terms of  $\Delta I_0$ , because the final number of available quanta is small, is one question, but if so it cannot be traced back to an original Poisson distribution in the initial flashes, at the retina, and consequently it cannot be said on any such basis that the essential variation in the data is due to fluctuations in the light rather than in the reacting organism.

<sup>24</sup> 1940-41, *J. Gen. Physiol.*, **24**, 635, 1941-42, **25**, 89, 293

<sup>25</sup> 1940-41, *J. Gen. Physiol.*, **24**, 505

<sup>26</sup> Hecht, S., Shlaer, S., and Pirenne, M. H., 1941-42, *J. Gen. Physiol.*, **25**, 819

<sup>27</sup> Barnes, R. B., and Czernay, M., 1932, *Z. Physik*, **79**, 436

<sup>28</sup> Cremer, H., 1937, Random variables and probability distributions, Cambridge Tracts, Mathematics and Mathematical Physics, No. 35, London, Cambridge University Press

The remaining point has to do with the form of the distribution of the frequency of 'successes' as a function of intensity near the threshold. The data specifically referred to in this discussion<sup>28</sup> are actually better described by a probability integral in  $\Delta I_0$  (not  $\log I$ ), which accords with our own experience. It is specifically in agreement with the requirement of our view concerning the mode of origin of logarithmic frequency distributions in visual excitation since for sufficiently short single flashes there is small opportunity for fluctuating performance in each excitable unit.<sup>9</sup> Under these circumstances it is to be expected that nothing like the 'reciprocity rule' for an inverse relation between exposure time and intensity critical for threshold should obtain, and extensive experimentation has shown us that it does not. Problems of the liminal photic energy for visual excitation have to be considered in terms of the properties of the assemblage of neural units involved.

It also accords with the meaning of results appearing when image area is varied since then the mean liminal exciting quantity of light ( $\Delta I_0 \times A \times t$ ) decreases with decrease of  $A$  down to a size so small that no exact image area can be estimated. Consequently, considerations of properties of threshold intensities in terms of energy and its fluctuations omit a factor vital to the whole situation. We therefore reject the suggestion that the fluctuations in critical intensities are not to be attributed to properties of the reacting organism.

The internal correlation manifest in the properties of  $\sigma_1$  can be estimated directly, with reasonably homogeneous data. Since the mean value of the ratio  $\sigma_1/I$  is independent of intensity, we can deal with the coefficients of variation collectively and write  $\sigma_1$  for  $\sigma_1/I$ . For repeated tests with the same population sample it is known<sup>29</sup> that

$$\sigma = \frac{\bar{\sigma}}{\sqrt{2N}} \sqrt{1-r} \quad (1)$$

where  $\bar{\sigma}$  is the mean of all the S.D.s,  $\sigma$  is the standard error of  $\bar{\sigma}$ , and  $r$  is the coefficient of internal correlation. (This is, of course, usually employed for estimating  $\sigma$  when  $r$  is known directly. Nothing in the derivation forbids reversing the argument to calculate  $r$  when  $\sigma^2$  is obtained from the data.) For coefficients of variation  $V$  less than 10 per cent, as in the present case,  $\sigma_r$  reduces to

$$\sigma_r = \frac{\bar{V}}{\sqrt{2r}}$$

so that we can proceed with (1). Putting (1) into the form in which we deal with  $\sigma$ s for the distributions of  $\sigma_1/I_m$  we have

$$\sigma_{11} = \frac{\bar{\sigma}_1}{\sqrt{2}} \sqrt{1-r} \quad (2)$$

<sup>28</sup> Cf. Peters, C. C., and van Voorhes, W. R., 1940 Statistical mathematical bases, New York and London: McGraw Hill.

and their

It is this  $r$  which we can use to obtain an invariant index of "organization" or *integration* among the neural units concerned in the determination of the flicker end-point along a given contour. It is independent of the level of  $I$  or  $F$ , and thus of the level of photic adaptation. Its numerical values in the present series of experiments are quite high, but show a systematic although complex dependence upon  $A$ ,  $t_L$ ,  $\lambda$ , retinal location, and kind of image. In other types of tests of sensory discrimination its magnitude changes in a striking way. When experiments are deliberately contrived to introduce non-homogeneity into the set of data considered, the value of  $r$  drops toward zero. Thus, for a mixed set of three separated series of measurements of  $\Delta I$  as a function of  $I_1$  (W J C, left eye, field  $12^\circ \times 12^\circ$ , at the fovea, white light) we have  $r = 0.101$ , whereas, for a single series  $r = 0.883$ . In repeated independent series of flicker determinations the degree of agreement with respect to  $r$  is indicated by such findings as these:  $r = 0.96, 0.97$  ( $3^\circ$  field at  $6^\circ$  temporal, white light, W J C, left eye),  $r = 0.98, 0.98$ , and  $0.97, 0.96$  for tests with our present field (iv). Under conditions as nearly alike as possible,  $r$  for flicker, with an undivided field, changes in a characteristic way with  $\lambda$ , from  $0.67$  (violet) to  $0.97$  (green).

From data previously printed we may illustrate the kind of result which  $r$  indicates. For unocular and binocular flicker tests, with two observers, we were able to show<sup>25</sup> that for the right and left eyes respectively the mean values of  $\sigma_1/I_m$  were lower for the right eye than for the left, and still lower for binocular excitation. The significance of these facts for the theory of "binocular summation" has been discussed<sup>25</sup>. It is of interest to consider the values of  $r$  computed from these measurements ( $6.13^\circ$  square, centered at the fovea, white light,  $t_L = 0.50$ ).

	<i>L</i>	<i>R</i>	<i>B</i>
W J C	0.917	0.854	0.817
E W	0.906	0.891	0.822

Thus, although the left eye ("dominant" in each case) gives a slightly higher value for  $\sigma_1/I_m$  than the right, and both eyes together give a value lower in the ratio of  $1/\sqrt{2}$  in the average,<sup>25</sup> the "internal coherence" of the measurements, in terms of their exhibition of scatter, is slightly higher for the left and quite definitely *lower* for both eyes used simultaneously. (For auditory  $L, R, B$  measurements  $r$  behaves in a quite different way.) This result is consistent with the finding, to be set forth subsequently,<sup>13</sup> that increase of flickered image area beyond a certain small size (*ca.*  $1.21^\circ \times 1.21^\circ$ ) characteristically causes  $r$  to drop. This may be complicated by the small but definite fall of  $r$  which typically goes with increase of  $t_L$ . In general, when image area, or light-time fraction, or wave length, is increased  $r$  rises to a maximum and then declines. A given series of measurements may fall on one or another branch of this kind of curve. In view of the correlated changes in  $F_{max}$  and in  $\sigma'_{log I}$  this is

taken to mean<sup>18</sup> that  $r$  is a function of the number of neural units involved and also of the density of elements of sensory effect they produce.

In a considerable number of series of measurements with various simple fields, on different parts of the retina, we find (as might be expected from the indications described in earlier papers<sup>20</sup>) that  $r$  is a declining function of  $\sigma_e$ . It has been shown that, when other things are equal, the scatter of  $\sigma_1$  increases directly with the value of  $F_{max}$ , and is thus a function of total number of elements of effect concerned. A test of this, which implies that in general  $r$  should rise and then decline as  $F_{max}$  increases over a sufficiently wide range, is particularly interesting in the case of subdivided fields. In our "pecten effect" experiments already described<sup>2</sup> there occurs a decrease of  $\sigma'_{log r}$  as well as of  $F_{max}$  as  $t_L$  is increased signifying (in terms of our analysis) that both number of units acting and mean frequency of contributed elements of effect from each unit are altered when  $t_L$  is varied. The curves for W J C are pitched at lower intensities ( $r'$  is smaller), are of lower  $F_{max}$ , and  $F_{max}$  and  $r'$  change more extensively when  $t_L$  is altered. This might lead to the conception that  $r$  should increase with  $t_L$  (and consequently with decline of  $F_{max}$ ) for the W J C data, which is found  $r$  rises steadily with fall of  $F_{max}$  for these curves from  $r = 0.68$  to  $0.86$ .  $F_{max}$  for E W at  $t_L = 0.90$  is the same as for W J C at  $t_L = 0.10$ , and the  $r$  constants there agree ( $0.86$ ) but for E W they fall to  $0.78$  at  $t_L = 0.10$  ( $F_{max} = 60.8$ ).

Applying these considerations to the measurements with our  $3^\circ$  subdivided square, where again  $\sigma_1$  and  $I_m$  are in rectilinear proportion we find that the values of  $\sigma_e$  are consistently lower when the square is subdivided

	$t_L$	= 0.10	0.50	0.90
$3^\circ \square$	$\log \bar{\sigma}$	= 3.755	3.867	3.883
$3^\circ \boxplus$	"	= 3.697	3.738	3.639

while the values of  $\bar{\sigma}$  may be a little lower, but not very significantly

	$t_L$	= 0.10	0.50	0.90
$3^\circ \square$	$\log \bar{\sigma}$	= 2.628	2.667	2.689
$3^\circ \boxplus$	"	= 2.623	2.596	2.609

Thus, although the mean value of the precision with which the end point is obtained is only slightly greater when the field is subdivided (by factors of 1.012, 1.178, and 1.202 as  $t_L$  is made 0.10, 0.50 and 0.90 respectively), the scatter of  $\sigma_1/I_m$  is decidedly lessened, by factors (in the same order) of 1.143, 1.346, 1.754. We do not regard the almost rectilinear increase of these factors with  $t_L$  to be necessarily accidental, but rather as pointing the way to a distinctly promising mode of inquiry.

The level of  $F_{max}$  (cf Fig 3) changes very little with  $t_L$  for the subdivided

<sup>20</sup> 1940-41 *J Gen Physiol* 24, 635 1941-42, 25 89 293

square, and the values of  $r$  do not change (0.97, 0.96, 0.98), they seem a little higher than with the simple square of field (i), 0.96, 0.95, 0.96, but we cannot hold that such differences are significant. A wider range of tests is necessary before we can conclude that (in the range of  $F_{max}$  where, as in the experiments with fields (i) and (ii),  $r$  is ordinarily at a maximum) an increase of the ("cone") slope constant without much change of  $F_{max}$  can affect the value of  $r$ . We can say, however, that for the same  $\sigma'_{\log I}$  the contours with field (iii), in section V, and field (ii) give a higher value of  $r$  for the field (ii) with lower  $F_{max}$ .

It is clear that these variational constants provide one means of estimating in a simple way the influence of additional factors affecting the internal coherence of data in an otherwise homogeneous set. For example, if conditions are found which permit the comparison of flicker curves brought to the same  $F_{max}$  by choice of  $t_L$ , and to the same slope by choice of image area<sup>15</sup>,  $r$  can be computed under the influence of lowered  $O_2$  pressure, medication, subdivision of the image, and the like. It should provide an index of the relative coherence of the state of neural integration governing the determination of the response. The properties of  $r$  confirm in an independent way the multivariate character of the situation controlling visual end-points, and illustrate once more why it is futile to found interpretive conceptions upon data derived from any single set of "standard" circumstances.

## V

Systematic investigation of the origin of effects of the type discussed in section III has been inviting. Certain steps have been taken in this direction<sup>18</sup>. Thus we have ascertained that the simple subdivision of a *small* field into two parts does not necessarily change the flicker contour if this is done in such a way as to produce only a small increase in the extent of the light/dark margin on the field. This could be pursued further. The promising but complex analytical possibilities presented by the flickering of a field in which parts are illuminated by one intensity while other parts are maintained at a different intensity (or  $\lambda$ ) may be mentioned. A firm approach to questions posed by the Gestalt psychology of perception is, of course, thus possible.

We are now concerned, however, with the exploration of the nature of the "pecten effect" in flicker<sup>3</sup>. The experiment discussed in section III has shown that mere subdivision of an illuminated field periodically illuminated by light sectored at a focus can cause the "cone"  $F - \log I$  curve to be steeper, change its relation to the light-time fraction  $t_L$  in the flash cycle, and alter its dependence of  $F_{max}$  on  $t_L$ . The simple splitting of the field (section III) does not, however, introduce into the dependence of the  $F - \log I$  contour on  $t_L$  the other major element of what we have recognized as the "pecten effect," namely the thorough upsetting of the normally simple, rectilinear dependence of  $r'$  on  $t_L$ <sup>3</sup>. This feature is, however, brought in, in a way which we have found sur-

prising, by a further elaboration of the kind of experiment concerned in section III

An illuminated field of  $10^\circ \times 10^\circ$  boundary at the retina was crossed by vertical (or horizontal) stripes. The field was centered at the fovea. Two such fields, already referred to as (iii) and (iv), are mainly concerned here. On (iii) there were three dark and four light vertical bars, each  $1.43^\circ$  wide. On (iv) there were six dark and seven light vertical bars, each  $0.77^\circ$  wide. The

TABLE III

Data for flicker response contours with different light time proportions, using a foveally centered square test field subtending  $10^\circ$  on a side at the retina, but divided by three equally spaced vertical opaque bars  $1.43^\circ$  wide, the four light bars thus produced being also  $1.43^\circ$  broad. White light, W J C., left eye  $n = 10$  at each point.

$f$ per sec	$t_L = 0.10$ $\log I_m \log P.E.$	0.25 $\log I_m \log P.E.$	0.50 $\log I_m \log P.E.$	0.75 $\log I_m \log P.E.$	0.90 $\log I_m \log P.E.$
2			6 1900 8 9123		
4			6 4344 8 8700		
6	7 4176 9 8307		6 7322 7 0812		7 9388 8 4068
8	7 7338 8 1844		6 0249 7 3426		6 2674 8 6642
10	6 0454 8 4604	6 9098 7 3605	6 2608 7 7894	6 4251 8 8221	6 6029 7 0178
12	6 3406 8 5274		6 6693 7 9193		6 8882 7 0638
15	6 5838 8 9686		6 8991 6 2488		6 1271 7 3971
18	6 9853 7 0384		4 3084 6 6410		6 5350 6 0799
20	6 2872 7 5541	4 1467 6 5627	4 6186 6 7621	6 5690 6 0889	6 7766 6 2280
			4 6006 6 8459		6 7806 6 1131
25	6 6281 6 0544		4 9440 5 2466		4 1626 6 5783
30	6 9802 6 3294	4 8710 5 1851	3 2638 5 6750	4 2830 6 7527	4 6349 6 8808
35	4 3287 6 7527		3 6229 4 0678		4 8620 5 3466
40	6 6986 6 9240	3 5544 5 7266	3 9609 4 6070	3 0338 5 5013	3 2014 5 6725
45	3 0068 5 2982		2 3068 4 6791		3 5714 4 0929
48	3 2667 5 7830		2 5824 4 9849		3 8418 4 1857
50	3 5993 4 0757	2 4870 4 8879	2 9034 3 4385	3 9527 4 4924	2 1881 4 6021
52	3 9882 4 3947		1 2931 3 7900		2 5666 3 0793
54	1 3251 3 8437		0 6188 1 0810		1 8068 3 9226
55	1 5628 0 0721				3 0951 1 6155

idea was to have, within the same total extent of image field, about the same illuminated area but about twice the dark/light perimeter in one field as in the other. It will be understood that in an exact sense these several conditions cannot really be satisfied. But it will also be apparent that for the purposes of the present account they are satisfied to an approximation which is sufficient.

It appeared in the course of the observations that when  $t_L$  was variously adjusted something peculiar was involved. This became the subject of very careful tests as to the possible existence of different kinds of flicker end points

TABLE IV

Data for flicker response contours with different light-time proportions using a square foveally centered test-field subtending  $10^\circ$  on a side at the retina, but divided by six equally spaced vertical opaque bars  $0.77^\circ$  wide, the seven light bars thus produced being also  $0.77^\circ$  broad. White light, W J C, left eye,  $n = 10$  at each point

$\frac{1}{\text{per sec}}$	$I_L = 0.10$ $\log I_m \log P.E.$	$0.25$ $\log I_m \log P.E.$	$0.50$ $\log I_m \log P.E.$	$0.75$ $\log I_m \log P.E.$	$p.90$ $\log I_m \log P.E.$
2		$\bar{6} \ 3166 \ \bar{8} \ 7111$	$\bar{6} \ 6566 \ \bar{8} \ 8993$ $\bar{6} \ 6427 \ \bar{8} \ 8284$		$\bar{6} \ 1430 \ \bar{8} \ 3939$
4		$\bar{6} \ 5527 \ \bar{8} \ 8319$	$\bar{6} \ 9909 \ \bar{7} \ 2377$	$\bar{6} \ 0820 \ \bar{8} \ 4342$	$\bar{6} \ 3836 \ \bar{8} \ 7004$
5			$\bar{5} \ 1473 \ \bar{7} \ 4032$		
6	$\bar{6} \ 0265 \ \bar{8} \ 2884$	$\bar{6} \ 9117 \ \bar{7} \ 5147$	$\bar{5} \ 2891 \ \bar{7} \ 5574$	$\bar{6} \ 3901 \ \bar{8} \ 7887$	$\bar{6} \ 6766 \ \bar{7} \ 0489$
8	$\bar{6} \ 3390 \ \bar{8} \ 6692$	$\bar{5} \ 2420 \ \bar{7} \ 5443$	$\bar{5} \ 5747 \ \bar{7} \ 7601$	$\bar{6} \ 7232 \ \bar{7} \ 1889$	$\bar{6} \ 9923 \ \bar{7} \ 1615$
9			$\bar{5} \ 7813 \ \bar{6} \ 0305$		
10	$\bar{6} \ 6980 \ \bar{7} \ 0014$	$\bar{5} \ 6909 \ \bar{6} \ 1366$	$\bar{4} \ 0212 \ \bar{6} \ 2638$ $\bar{4} \ 0993 \ \bar{6} \ 4370$ $\bar{4} \ 0094 \ \bar{6} \ 2076$	$\bar{5} \ 0715 \ \bar{7} \ 4736$	$\bar{5} \ 3641 \ \bar{7} \ 6642$
12	$\bar{6} \ 9699 \ \bar{7} \ 2736$	$\bar{5} \ 9602 \ \bar{6} \ 3093$	$\bar{4} \ 3688 \ \bar{6} \ 6823$ $\bar{4} \ 2591 \ \bar{6} \ 5297$	$\bar{5} \ 3243 \ \bar{7} \ 6220$	$\bar{5} \ 6325 \ \bar{7} \ 9719$
15	$\bar{5} \ 3183 \ \bar{7} \ 6981$	$\bar{4} \ 2955 \ \bar{6} \ 7096$	$\bar{4} \ 6195 \ \bar{6} \ 9507$ $\bar{4} \ 6345 \ \bar{6} \ 8783$ $\bar{4} \ 6168 \ \bar{6} \ 8442$ $\bar{4} \ 8774 \ \bar{5} \ 2219$	$\bar{5} \ 6829 \ \bar{6} \ 0879$	$\bar{5} \ 9820 \ \bar{6} \ 4078$
17					
18	$\bar{5} \ 7124 \ \bar{6} \ 0083$	$\bar{4} \ 7033 \ \bar{5} \ 2473$	$\bar{3} \ 0374 \ \bar{5} \ 3021$ $\bar{3} \ 0191 \ \bar{5} \ 2923$	$\bar{4} \ 0842 \ \bar{6} \ 5098$	$\bar{4} \ 3820 \ \bar{6} \ 6847$
20	$\bar{5} \ 9585 \ \bar{6} \ 2042$ $\bar{5} \ 9699 \ \bar{6} \ 4996$	$\bar{4} \ 9405 \ \bar{5} \ 3635$ $\bar{4} \ 9138 \ \bar{5} \ 2884$	$\bar{3} \ 2925 \ \bar{5} \ 5387$ $\bar{3} \ 2595 \ \bar{5} \ 4550$ $\bar{3} \ 2579 \ \bar{5} \ 6329$ $\bar{3} \ 2993 \ \bar{5} \ 5498$ $\bar{3} \ 2472 \ \bar{5} \ 5122$	$\bar{4} \ 3632 \ \bar{6} \ 5387$ $\bar{4} \ 3841 \ \bar{6} \ 5584$	$\bar{4} \ 6221 \ \bar{6} \ 7950$ $\bar{4} \ 6294 \ \bar{6} \ 9695$
25	$\bar{4} \ 3340 \ \bar{6} \ 7595$ $\bar{4} \ 3591 \ \bar{6} \ 6989$	$\bar{3} \ 2655 \ \bar{5} \ 5813$ $\bar{3} \ 2653 \ \bar{5} \ 6839$	$\bar{3} \ 6965 \ \bar{5} \ 9429$ $\bar{3} \ 6145 \ \bar{5} \ 9546$ $\bar{3} \ 6142 \ \bar{5} \ 8637$ $\bar{3} \ 6188 \ \bar{4} \ 0330$	$\bar{4} \ 7423 \ \bar{5} \ 0857$ $\bar{4} \ 7570 \ \bar{5} \ 1854$	$\bar{3} \ 0441 \ \bar{5} \ 3861$ $\bar{3} \ 0693 \ \bar{5} \ 4108$
30	$\bar{4} \ 7560 \ \bar{5} \ 1824$	$\bar{3} \ 6502 \ \bar{5} \ 9995$	$\bar{2} \ 0519 \ \bar{4} \ 2574$ $\bar{2} \ 0580 \ \bar{4} \ 1879$ $\bar{2} \ 0374 \ \bar{4} \ 3021$ $\bar{2} \ 0195 \ \bar{4} \ 1752$	$\bar{3} \ 1007 \ \bar{5} \ 5098$	$\bar{3} \ 3936 \ \bar{5} \ 7681$
35	$\bar{3} \ 1222 \ \bar{5} \ 3001$	$\bar{2} \ 0077 \ \bar{4} \ 4159$	$\bar{2} \ 3802 \ \bar{4} \ 7288$ $\bar{2} \ 3829 \ \bar{4} \ 6311$ $\bar{2} \ 4591 \ \bar{4} \ 8096$	$\bar{3} \ 4673 \ \bar{5} \ 8637$	$\bar{3} \ 7553 \ \bar{4} \ 0038$
40	$\bar{3} \ 4286 \ \bar{5} \ 8420$ $\bar{3} \ 3051 \ \bar{5} \ 6549$	$\bar{2} \ 3251 \ \bar{4} \ 7956$ $\bar{2} \ 3084 \ \bar{4} \ 6060$	$\bar{2} \ 7171 \ \bar{3} \ 0094$ $\bar{2} \ 7254 \ \bar{3} \ 0513$ $\bar{2} \ 7142 \ \bar{3} \ 0506$ $\bar{2} \ 7101 \ \bar{3} \ 0038$	$\bar{3} \ 7918 \ \bar{4} \ 1658$ $\bar{3} \ 7824 \ \bar{4} \ 2599$	$\bar{2} \ 0338 \ \bar{4} \ 4063$ $\bar{2} \ 0599 \ \bar{4} \ 4468$

TABLE IV—Continued

$F$ per sec	$t_L = 0.10$ $\log I_m \log P.E.$	$0.25$ $\log I_m \log P.E.$	$0.50$ $\log I_m \log P.E.$	$0.75$ $\log I_m \log P.E.$	$0.90$ $\log I_m \log P.E.$
45	3 7418 4 1518	2 6302 4 9781	1 0526 3 3986 1 0500 3 3955 1 0704 3 1647	2 1486 4 6041	2 4055 4 7208
48	3 9517 4 2028	2 7811 3 0468	1 2499 3 5530 1 2646 3 5773	2 3866 4 7601	2 7186 3 0678
50	2 2997 4 7345	1 0484 3 4123	1 6101 3 6839 1 6156 3 8324 1 6294 3 9554	2 6503 4 9202	2 9983 3 3512
51			1 6170 3 9639		
52	2 6187 4 8669	1 4643 3 8078	1 9312 2 3438 1 9024 2 1994	1 0792 3 3301	1 4041 3 7520
53			0 3008 2 5454	1 9054 2 3228	0 7453 1 5432
54	1 0650 3 3581	0 3740 2 6791	0 6878 1 0812	3 2904 1 5874	
55	0 4794 2 9032	1 3128 1 3301	1 2646 1 4550 1 2521 1 4001 0 9734 1 3766		

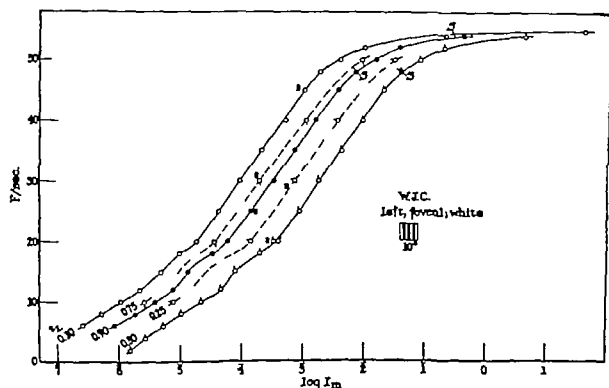


FIG. 7. Flicker contours for a square field  $10^\circ$  on a side over-all but subdivided into seven vertical bars  $1.43^\circ$  wide alternately illuminated and opaque centered at the fovea. Note that the curves for  $t_L = 0.75$  and  $0.90$  are at lower intensities than that for  $t_L = 0.25$ . The contours are quite steep but clearly of the same general slope. The 3-bar symbol on each curve indicates the level at which the field was recognized as barred. See text. Data in Table III.



which might be confused. We shall return to this presently. But it became clear that this kind of complication did not really enter. The peculiarity had to do predominantly with the location on the  $\log I$  axis of the contours at  $t_L = 0.75$  and  $0.90$ . Precisely as in our experiments with moving vertical stripes on a barred field, the contours for  $t_L = 0.75$  and  $0.90$  were shifted bodily to much lower positions on the intensity scale, but in the present case with no change of slope constant and with very slight change of  $I_{max}$ . This completes the objective evidence justifying the view that at least three independent parameters are required for the formulation of the (simplex) flicker curve,<sup>31</sup> since each of our  $\tau'$ ,  $\sigma'_{log I}$ , and  $I_{max}$  parameters can thus be experimentally changed in uncorrelated ways. It also appears that three such parameters are sufficient.

The measurements for the contours with fields (iii) and (iv) are collected in Tables III and IV, and are shown in Figs. 7 and 8. The curves for the more finely subdivided field are pitched at a higher intensity level ( $\tau'$  nearly 1 log unit greater for field (iv)—cf. Fig. 10), but show qualitatively the same sort of dependence on  $t_L$ .  $I_{max}$  changes more with (iv) as  $t_L$  is increased. As shown in Fig. 9 the slope constant  $\sigma'_{log I}$  for (iv) is less than for (iii), i.e., the slope is greater. Here, as in section III, this automatically brings about an increase in the size of the "rod" contribution in (iv), in fact nearly doubles it, although it appears at a higher intensity (cf. Figs. 1 and 2). Again we point out that such relationships cannot be rationalized in simple terms of an available population of illuminated retinal receptor units with individually fixed intensity thresholds. In (iv) the illuminated image area (52.9 square degrees) is actually less than that (57.2 square degrees) for (iii), although  $\sigma'_{log I}$  is greater, so the "rod" effect cannot be accounted for on this basis.

The lengths of lines of separation between light and dark portions of the barred fields, however, are (iii) =  $91.11^\circ$ , (iv) =  $150.78^\circ$ , in the ratio 1/1.65. The "cone" slope constants ( $1/\sigma'_{log I}$ ) are in the ratio 1/1.2. In the experiment of section III, doubling the dark/light perimeter increases the slope in the ratio 1/1.43.

The very considerable increase in ("cone") slope produced by increasing the subdivision of the field is not confined to white light, but is shown also with separated portions of the spectrum. Data with blue and red lights are given in Fig. 11 (Table V), for  $t_L = 0.50$ . We have pointed out that with simple fields  $I_{max}$  and  $\tau'$  occupy an intermediate position for a *white*, as contrasted with the positions (on the same brightness or energy-at-cornea scale for  $\tau'$ ) taken by the opposite ends of the spectrum filtered from it<sup>31</sup>. The properties of  $\sigma'_{log I}$  for different spectral regions are not inconsistent with the view that *white* is not a simple "addition" of primaries, but represents a sort of integrative synthesis<sup>31</sup>. In general, for simple fields, the  $F - \log I$  contour at the same  $t_L$  is with *white*

<sup>31</sup> 1941-42, *J. Gen. Physiol.*, 25, 89, 293, 1943-44, 27, 119

intermediate ( $r'$ ) between that for *blue* and *red*. The data of Fig 11 show that by suitable subdivision of the test field this order can be radically disturbed. On a scale of brilliance intensity the steady light values for the flash intensities adequate to evoke flicker with *blue*, *red*, *white* assume a different order when the field is suitably subdivided. This is also true if the intensities are put on an

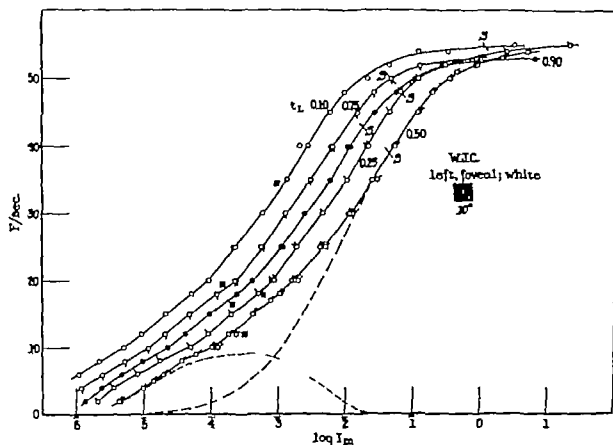


FIG 8 As in Fig 7 a  $10^\circ$  square field centered at the fovea, but divided into thirteen alternating light and dark vertical bars  $0.77^\circ$  wide. The curves are steeper than those of Fig 7 (cf Fig 9). Data in Table IV. The contours at  $t_L = 0.75$  and  $0.90$  are, as in Fig 7, so shifted that they fall between those for  $t_L = 0.10$  and  $0.25$ . By comparison with the curves of Fig 7 those here shown are located at higher intensity levels (cf Fig 10). Above  $\log I = ca\ 4.6$  the illuminated fields are speckled. The intensities (barred symbol) at which the barred pattern is resolved on the contour, are, however, about the same as in Fig 7. At and above the flash intensities marked *S* the illuminated bars are smooth.

energy basis. At this particular value of  $t_L$  ( $\approx 0.50$ ),  $r$  for *B*, *W*, *R* is respectively  $0.99$ ,  $0.97$ ,  $0.95$ ; the differences in  $\sigma$  are more impressive  $3.372$ ,  $3.699$ ,  $3.784$ . These, like the foregoing, agree with the apparent order of  $F_{max}$  while the differences detectable in  $\sigma'_{log}$  are insignificant. It is not without value for the conception of the multivariate control of the quantitative properties of the flicker contour that comparatively simple subdivision of the field *should* alter the order of relative effectiveness of different wave length.

According to the view required by the data of the flicker contours we have supposed that (section III) a primary part may be played by the existence of lines of separation between light and dark areas in the flickered field. The striking modifications in the  $I - \log I$  curves by simple subdivision of the image area are consistent with this notion. We have been required to assume that the existence of contrast edges, even when not visually resolved, serves to enhance the number of neural units concerned in the discrimination of

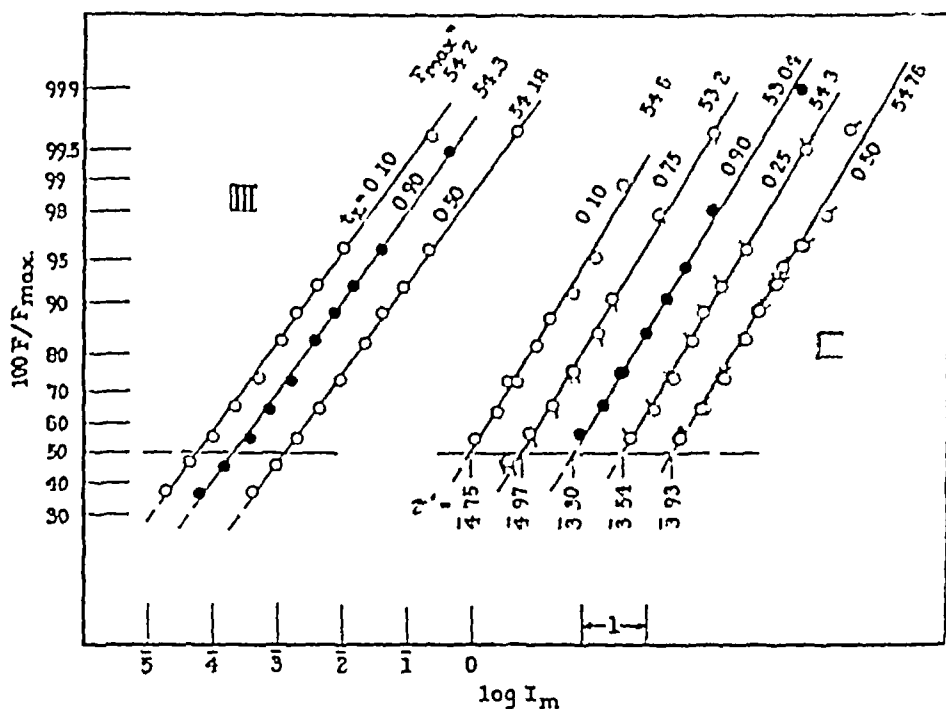


FIG. 9. The higher intensity segments of  $F - \log I$  contours in Figs. 7 and 8, shown on a probability grid. Only the upper 50 per cent or so is uncomplicated by the "rod" contribution, but it is significant that for each set the slopes are uniform.

flicker, although total illuminate area is the same, and even though the whole field concerned subjectively flickers uniformly at the critical intensity.

In the data of our fields (iii) and (iv) it has to be emphasized that, as in the case of field (iii) (section III), the effect in question is definitely at work at flash intensities, let alone at brightnesses-at-fusion, well below those adequate for subjective recognition of the fact that the field is actually subdivided. At the moment, there are two chief aspects of interest in this situation. The first has to do with the argument for the essential unity of the organic mechanism determining the form of the flicker contour despite the manifestations of visual duplexity. We have already spoken of the importance of this conception as

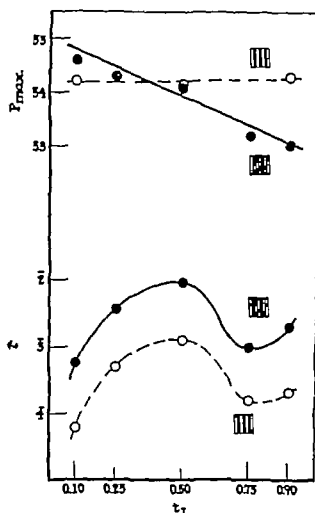


FIG. 10 The values of  $F_{max}$  and of the abscissa of inflection  $\tau'$  obtained from Fig. 9 are shown as functions of  $t_L$ , for the curves of Figs. 7 and 8. The structure of the flickered fields is indicated by the barred symbols.

TABLE V

Conditions as in Table IV but using red light (two independent series) and  $Nac$   $t_L = 0.50$  (Intensities in millilamberts, by matches with white.)

$F$ per sec.	$t_L = 0.50$ Red		$t_L = 0.50$ Blue	
	$\log I_m$	$\log P.E._1$	$\log I_m$	$\log P.E._1$
20	4 6415	3 1117	5 1172	7 4667
	4 6598	3 9748		
25	3 0020	3 4241	5 5097	7 9051
	4 9963	3 2916		
30	3 4240	3 7272	5 9501	6 2187
	3 4309	3 8960		
35	3 8197	4 1343	4 2758	6 5901
	3 8101	4 3240		
40	2 1019	4 3261	4 5397	6 8716
	2 1386	4 5074		
45	2 4296	4 8989	4 8578	3 2005
	2 4388	4 9247		
48	2 6639	3 0714	3 0820	3 4354
50	2 9565	3 1484	3 3669	3 6639
52	1 4466	3 9721	3 7820	3 1351
54	0.2972	2 7095		
55			1 3418	

rationalizing the quantitative behavior of the scotopic section of the curve under various conditions both mild and drastic. The second aspect of theoretical importance concerns the relations of flash intensity, flash brightness, and especially of fused (Tilbot) brightness in flickered light to "visual acuity." This is important in a number of ways which should have been examined a good while ago but seem to have been ignored. We are concerned here to indicate that the data provide a method for the experimental separation of effects due to subjective *brightness* from those due simply to *intensity*. Thus, on the curves of our "pecten" experiment the cross-harring of the field—as perceptible at the same *flash intensity* down to a light-time fraction of 0.25 ( $L/W$ ) or 0.50

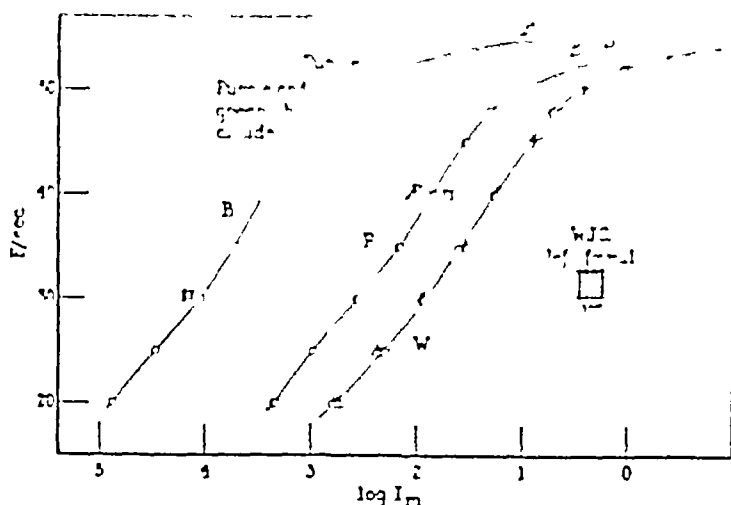


FIG. 11 Thicker contours,  $t_L = 0.50$ , with the  $10^\circ$  square subdivided into seven illuminated strips, centered at the fovea, for *blue* and *red* (Table V), compared with *white* on the same (steady light) brightness scale. The points at which the illuminated fields become subjectively smooth, exhibit color, and are visually resolved as barred, are indicated.

(W J C) In the experiment of section III the bars subdividing the field were just visible (on the contours) at a flash intensity of  $\bar{4}.80$  log units (millilamberts), regardless of the light-time fraction, and thus independent of the fused brightness. (Incidentally, for  $t_L > 0.50$ , this means that in the tests with the moving stripes<sup>3</sup> the field is resolved at the *same* flash intensity regardless of whether there is any sign of involvement of the "cone" curve.) Consequently, we are dealing primarily with effects due to the physical intensity of a flash, rather than to its duration or to the subjective brightness level. For comparatively simple fields, the constancy of the flash intensity for visual resolution in flickered light<sup>32</sup> extends to light-time fractions below 0.10, although for more

<sup>32</sup> 1943-44, *J. Gen. Physiol.*, 27, 119.

complex fields this constancy may fail somewhat below  $t_L = 0.25$ , while even so not obeying the course of the Talbot brightness. A more extensive examination of this matter has been made, and will be described elsewhere. Fields (iii) and (iv), with four and seven illuminated vertical bars respectively, were visually resolved (on the  $F - \log I$  contours) at a log flash intensity which declined rectilinearly with increasing  $t_L$  (Fig. 12)

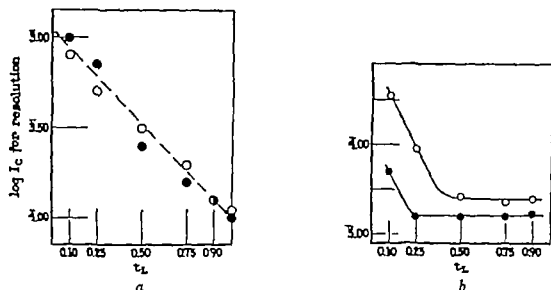


FIG. 12. Illustrating the complex dependence of visual resolution in flickered light upon flash intensity  $I$  at different light time fractions on the flicker contours.

(a) Open circlelets, 3-barred pattern (field (iii)); solid circlelets 6-barred pattern (field (iv)). The mean flux, corresponding to the Talbot brightness is very nearly approximated at the point of resolution: thus reducing  $t_L$  to 0.10 requires nearly ten times the flash intensity necessary with steady light.

(b) Flash intensity vs  $t_L$  for the resolution of the barred pattern of our 'pecten experiment';<sup>23</sup> open circlelets W J C, solid dots E.W. Here, over a good range resolution of the pattern is determined by flash intensity alone independent of  $t_L$ .

Thus there are conditions under which resolution of a more finely subdivided field is possible with a lower flash intensity even when the length of the subdivisions is the same. The rôle of the latter factor is easily demonstrated.<sup>24</sup> It has been known<sup>24</sup> that the presence of a nearby contrast border can affect the visual resolution of a given such border. The flicker data prove that phenomena of this kind involving pronounced integration of visual functioning can operate even when contrast as such is not perceived (i.e., below the flash intensity required for resolution of the barred pattern).

One aspect of the integrative action of an increased number of effective neural units is reflected in the associated variational indices, as we have already sug-

<sup>23</sup> A following paper deals with certain of these questions.

<sup>24</sup> Cf. Bartley S. H. 1941 *Vision: a study of its basis*, New York: D. Van Nostrand Co. Inc., Chapter X.

gested. In the data of tables III and IV,  $\sigma_1/L_m$  is statistically constant. The values for  $\bar{\sigma}$  and for  $\sigma_*$  here differ relatively little, although those for the 1-bar field (iii) may be slightly higher. They are smaller, however, than one would be led to expect for a simple field of the same illuminated area. For a square  $6^\circ$  field at the fovea, the values of  $\sigma$  are not different significantly, but those for  $\sigma_*$  are larger with the  $10^7$  field by the average factor of 1.74, although the fields (iii) and (iv) are half again as large, and  $L_{max}$  is decidedly higher, and we find that  $\sigma_*$  increases when the image area of a simple square is enlarged in this way. The constant  $r$  is consistently larger by a little for the 7-bar field (iv) than for the 4-bar field (iii), the latter having less than two thirds of the light-dark perimeter in the former (Fig. 13). This is quite striking because of the general relation previously described for simple fields between  $L_{max}$  and  $r$ .

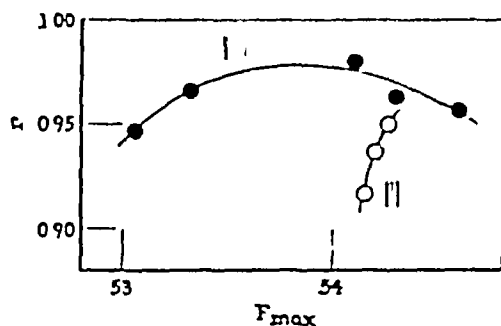


FIG. 13. The values of  $r$  in the expression  $\sigma_*/\sigma\sqrt{2} = \sqrt{1-r}$  (see text), as a function of  $F_{max}$ , for the series of flicker contours with fields (iii) and (iv).

We conclude, therefore, that the degree of integration involved in the recognition of visual flicker, as a function of flash frequency and intensity, is decidedly enhanced by the imposition of image forms (subdivision into stripes) such that more visual units are involved together with a reduction in the effective contribution of elements of neural action from each unit.

## VI

The peculiar transposition of the  $t_l$  0.75 and 0.90 contours in the data of section V led us to inquire if we were being in some fashion misled by the occurrence of more than one intensity critical for subjective flicker, at a given  $F$ . It is true that under certain conditions  $t_L = 0.50$  is a critical light-time fraction, as Porter<sup>35</sup> found for fixed illumination reflected from a spun sector disk, this result, for which an explanation has been offered,<sup>36</sup> does not enter here. Be-

<sup>35</sup> Porter, T. C., 1898, *Proc. Roy. Soc. London*, 63, 347.

<sup>36</sup> 1937-38, *J. Gen. Physiol.*, 21, 313, 463; Pieron, H., 1935, *Ann. Psychol.*, 35, 1.

sides, it is desirable to be able to account for the fact that the curve of  $\tau'$  as a function of  $t_L$  exhibits a minimum at  $t_L = 0.75$  (Fig 10)

In tests of visual acuity with grating patterns it has been found that a difference in resolvability appears when the grating stripes are at different angles to the vertical.<sup>27</sup> For our field (iv) we find that this difference likewise appears under flickered light (Table V, Fig 14), and also that the whole flicker contour is displaced toward slightly higher intensities when the barred field is turned

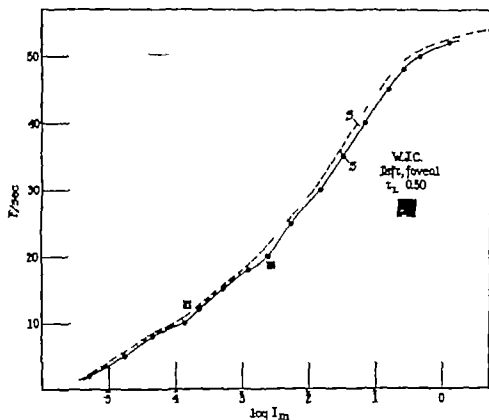


FIG 14 Flicker contour for 6-barred field (iv) with stripes vertical (dashed line, from Fig 8  $t_L = 0.50$ ) compared with that for the same field with the stripes rotated  $90^\circ$  horizontal

The point above which the horizontally barred pattern was resolved is indicated by the symbol well above the level for the vertical bars. At S the illuminated areas became smooth. See text

with the stripes horizontal (field (v)). We doubt that gross ocular astigmatism can account for this difference, since it persists when the very slight astigmatism is suitably corrected. A more natural explanation may be found in the neural structure of the foveal region ("retinal astigmatism"). This is described as receiving rather distinct upper and lower groups of nerve fibers.<sup>28</sup>

<sup>27</sup> Shlaer S *J Gen Physiol* 1937-38 **21**, 165

<sup>28</sup> Duke-Elder W S *Textbook of ophthalmology* St Louis, C V Mosby Co 1938 **1**, 262 Polyak, S L., *The retina* Chicago University of Chicago Press 1941 Fig. 43



The suggestion is that flicker may be a little less easily perceived when groups of neighboring receptor units are simultaneously illuminated in the same manner, if their fiber connections remain together. Calculation of the  $r$  constant

TABLE VI

Illustrating the relation between flash frequency and flash intensity critical for the appearance of the " $\gamma$  movement effect," conditions as in Table V for  $t_L = 0.75$ . The  $\gamma$  movement thresholds are of course obtained only above flash intensities at which the illuminated bars are separately visible, see text

$F$ per sec	$t_L = 0.75$	
	$\log I_m$	$\log P F_1$
20	5.7859	5.9160
25	4.1309	6.4788
30	4.6298	6.9326
35	4.8813	5.1306
40	3.2127	5.6238
45	3.5371	5.8284
48	3.7367	4.0200
50	2.0269	4.3191
52	2.4200	4.5834
54	1.2709	3.5251

TABLE VII

An exceptional series of observations under the conditions specified in Table V for  $t_L = 0.50$ , involving the " $\phi$  effect," see text

$F$ per sec	$t_L = 0.50$	
	$\log I_m$	$\log P F_1$
20	3.4763	5.7281
25	3.8308	4.2444
30	2.1959	4.4441
35	2.5572	4.9065
	2.5526	4.7402
40	2.8596	3.1561
45	1.2156	3.5297
	1.2388	3.4890
48	1.5173	3.7681
	1.4965	3.7193
50	1.8799	2.0079
	1.8511	2.1172
52	0.2804	2.5742

from the flicker data shows that it is little, but significantly, lower (0.966 vs 0.980) for the horizontal stripes. The estimated  $F_{max}$  is also a little lower. This would indicate an organizational factor, which might of itself be a function of the light-time fraction.

We have sought diligently to see if more than one flicker end point could be found on the intensity scale with  $F$  and  $t_L$  fixed, but we have not found any. It is true that with the barred pattern (iv) visual disturbances of certain interesting kinds are easily recognizable at other critical intensities when the bars are almost or quite resolved, but there is no difficulty in distinguishing them from the occurrence of flicker. The most interesting of these we have regarded as an example of " $\gamma$ " apparent movement. This most obvious at  $t_L = 0.75$ , consists in a pulsatile widening and contracting of the illuminated stripes,<sup>29</sup> at a rate lower than that of the flashes. The end point is easily

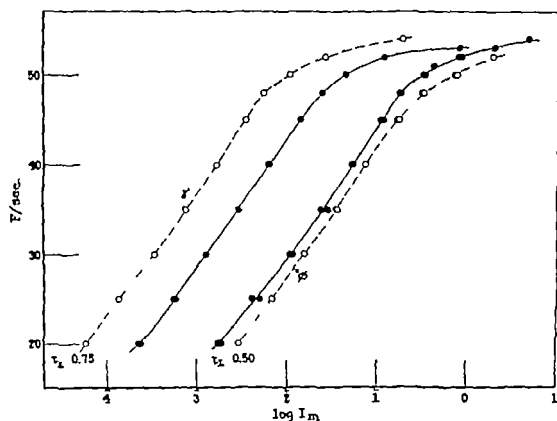


FIG. 15 Upper portions of flicker contours for  $t_L = 0.50$  and  $0.75$ , solid circles from Fig. 8, with corresponding curves for " $\gamma$ " movement and " $\phi$ " movement. See text.

recognized. As shown in Fig. 15, the " $\gamma$ " effect provides a contour similar to that given by the flicker end point, although at lower intensities and with a higher  $F_{max}$  (54.5 vs 53.2 for flicker). Analysis of the curves in Fig. 15 shows that  $\sigma_{log I}$  is not different for these " $\gamma$ " data. It is of some interest that for the " $\gamma$ " set the relative variation ( $\sigma_1/I_m$ ) is lower than for flicker at  $t_L = 0.75$  by a factor of 0.835, and the scatter of this ratio ( $\sigma$ ) is also lower, by the factor 0.867, so that  $r$  is not essentially different, being 0.964 vs 0.966.

The conclusion that the same neural units, to the same number, are con-

<sup>29</sup> Cf. Bartley S. H., 1941 Vision: a study of its basis. New York, T. Co. Inc., Chapter VII.

cerned as in the recognition of flicker, although the subjective effect used is not the same, is supported by other series of measurements based upon what we regard as another kind of apparent movement which we may for convenience but without prejudice label the "φ" type.<sup>22</sup> This sort of "movement" in the subdivided visual field may be described as a kind of pulsatile pseudomovement, running from side to side of the field. We cannot be entirely certain that it is independent of eye movements. It appears at a flash intensity slightly but systematically above the unmistakable flicker end-point. In our experience with field (iv) it is best developed at  $t_L = 0.50$ , and its use as an end point gives a contour at slightly higher intensities than for flicker (Fig. 15), although again  $\sigma'_{\log I}$  is the same,  $I_{max}$  is a little lower than for flicker at the same  $t_L$  (53.05 vs 51.16),  $\sigma/I_m$  is a little lower,  $\sigma_e$  still lower,  $r$  is the same (0.977 vs 0.980). It may be remarked that, just as for flicker when  $t_L$  is varied,  $r'$  and  $I_{max}$  tend to change reciprocally.

In connection with the relation of (critical) flicker to other subjective phenomena we should note that a certain independence of the properties of the contours can be demonstrated as concerns brightness,<sup>23</sup> visual resolution of the field structure,<sup>24</sup> color,<sup>25</sup> and other phenomena. Thus, in Figs. 2, 7, 8, and 14 points along the contours are indicated at which the respective fields are no longer "speckled" or "frosted" but become "smooth" and evenly illuminated, so also in Fig. 11 these points are shown, and the color thresholds. For the "γ" curve of Fig. 15 the lighted bars appear smooth only above  $\log I_m = ca. \bar{1}$ , and the bars are visually resolved at about  $\log I_m = 4.0$ , just as for the normal flicker end-point at  $t_L = 0.75$ . The levels of occurrence of these effects, while related in interesting ways to  $t_L$ , are not associated in any manner with the presence of singularities on the  $I - \log I$  curves.

To account for the relative positions of the  $t_L$  contours with the barred fields we must turn to properties of the "edge effect." The reality of this effect is attested (1) by the systematic changes in the shapes of the curves which cannot be accounted for by changes in image area (sections III and V), and (2) by properties of the variational indices. It is also consistent with the fact that, subjectively, arrival at the critical intensity produces a more pronounced flicker along the image edges (although the whole illuminated area flickers simultaneously). To account for the non-specific nature of the shifts of  $I - \log I$  curves with change of temperature and of  $t_L$  it has been proposed<sup>26</sup> that the flash intensity critical for flicker results from the appropriate relation between the effects of flashes and of the decay of their after-effects. With the barred fields we have indication that the number of neural units concerned is large ( $\sigma'_{\log I}$  is small). The fact that  $I_{max}$ , although not very high, changes so very little with  $t_L$  (as with field (ii) also) must be taken to mean that, although the

<sup>20</sup> 1941-42, *J. Gen. Physiol.*, **25**, 89, 293, 369, 1943-44, **27**, 119

<sup>21</sup> 1936-37, *J. Gen. Physiol.*, **20**, 393, 1937-38, **21**, 313

mean contribution of elements of effect per neural unit is small it tends to decrease with  $t_L$  less than might be expected. It is known that the relative expansion and contraction of an illuminated bar in  $\gamma$  apparent movement is a function of  $t_L$ , and we have already pointed out that with our fields (iii) and particularly (iv), it is a maximum (in our series) at  $t_L = 0.75$ . The conception then might be that the "edge" or bar effect with which  $\gamma$  apparent movement is associated, and of which the latter is one expression, operates in such a way as to contribute elements of effect from the same units in addition to those ordinarily concerned in the recognition of flicker and that this contribution is more marked above  $t_L = 0.50$ . To the extent that let us say a symmetrical balance of the expanding and decaying phases of the  $\gamma$  apparent movement must be achieved for effective reinforcement of the ordinary flicker effect, this could well result in a lower critical intensity for the net result with a given  $F$  at the level of  $t_L$  most efficient for the ' $\gamma$ ' effect. Ordinarily with simple (rectangular) fields, above an image area of ca. 0.73 square degrees, the change of  $r'$  per unit change of  $t_L$  ( $= \Delta r' / \Delta t_L$ ) is found to decrease steadily as the image area is increased.<sup>12</sup> This is correlated with changes in  $\sigma'$  and in  $F_{max}$  signifying an increase in number of units concerned and a relative diminution in the number of elements per unit required to evoke flicker. In our field (ii)  $\Delta r'$  is considerably reduced by comparison with (i), which is consistent with the foregoing. For the striped fields (iii) and (iv) the behavior of  $r'$  seems to show that the number of elements of effect per neural unit required to be involved at the end point is reduced by the "edge effect" especially at lower values of  $t_L$ . The " $\gamma$ " phenomenon appears to reverse the change of  $r'$  with increase of  $t_L$  when it becomes a sufficient factor just beyond  $t_L = 0.50$ . At  $t_L = 0.90$  the " $\gamma$ " effect is subjectively not so pronounced under our conditions a lesser contribution from it is thus to be expected, and therefore  $r'$  must increase in the usual way relative to the 0.75 contour.

This interpretation is of course tentative, but some interesting tests can be based upon it.

## VII

### SUMMARY

Flicker contours for a square image of  $3^\circ$  visual angle centered  $6^\circ$  on the temporal side of the fovea, the light sectorized at a focus, are strikingly modified if the same illuminated area is arranged in four squares separated by a narrow opaque cross. The "cone" curves are made much steeper, and their abscissae of inflection ( $r'$ ) are at higher intensities,  $F_{max}$  is not greatly changed, but alters less with change of light time fraction in the flash cycle ( $t_L$ ). This modification is accompanied by a great enlargement of the scotopic segment of the duplex curves consistent with the theory of the integrative relations of neural effects in the two groups of units involved. The changes are not consistent with the



# THE STRUCTURE OF THE COLLODION MEMBRANE AND ITS ELECTRICAL BEHAVIOR

## VIII. QUANTITATIVE STUDIES CONCERNING THE ACIDIC PROPERTIES OF COLLODION AND THEIR CORRELATION WITH MEMBRANE STRUCTURE AND ACTIVITY

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### I

In preceding papers<sup>1-3</sup> it was shown that the electrochemical behavior of collodion membranes in solutions of strong, weakly adsorbable electrolytes is due to the presence of acidic impurities in the collodion. Pertinent quantitative data were obtained from base exchange studies.<sup>4</sup> No regular correlation was found between electrochemical activity<sup>1,2,4</sup> and base exchange capacity. A measurable base exchange capacity seems to be associated always with good or high electrochemical activity but base exchange capacities too low to be definitely measurable with the methods used were found with collodion preparations of high as well as with low electrochemical activity.

The very low base exchange capacities even of very active preparations could be due to a very low content of acidic groups or to a lack of availability for base exchange of the majority of them. Thus, it became of interest to obtain quantitative information on the equivalent weight of collodion preparations of different electrochemical activity and to compare it with their base exchange capacity. In this way one could hope to obtain valuable information on the relative availability of the acid groups and on the submicroscopic, micellar structure of collodion fibers or collodion membranes from different preparations.

On certain aspects of this problem we already have some information. Work from this laboratory indicates that the base exchange capacity corresponds to but a fraction of all the acid groups present in collodion. Furthermore we already know what the rate at which base exchange occurs varies with different collodion preparations, faster base exchange being indicative of relatively open structure.<sup>4</sup>

<sup>1</sup> Sollner K. and Abrams, I. *J Gen Physiol.*, 1940 24, 1

<sup>2</sup> Sollner K. Abrams I. and Carr C. W., *J Gen Physiol.*, 1941 24, 467

<sup>3</sup> Sollner K. Abrams, I. and Carr C. W. *J Gen Physiol* 1941 25 7

<sup>4</sup> Sollner K. Carr C. W. and Abrams, I., *J Gen Physiol* 1942 25, 1



ton<sup>7</sup> Wooten and Ruehle<sup>8</sup> and Ruehle.<sup>9</sup> (See also below<sup>10</sup>) The titration is performed with a solution of alkali hydroxide in an organic solvent. The electrode which responds to the change in acidity is a quinhydrone electrode; some quinhydrone is added to the collodion solution, with a bright platinum wire dipping into it. The reference electrode is a calomel half cell which is connected in the usual manner by means of a potassium chloride-agar bridge to the solution. To increase the conductance of the titrated solution some saturated solution of lithium chloride in alcohol is added. Nevertheless, the ohmic resistance of the system is rather high and an electron tube voltmeter must be used. For this purpose we have used the volt scale of a commercial (Leeds and Northrup) glass electrode.

We have tested a number of different solvents and solvent mixtures for their suitability for our special problem. Some of the solvents recommended in the literature are not obtainable in a sufficiently pure state and can be purified only with considerable difficulty. On account of their ready availability in great purity, we finally worked with acetone and absolute alcohol, mixtures of which show excellent solvent properties for collodion.

To obtain satisfactory results it is necessary to take certain precautions. The quinhydrone should be carefully recrystallized and stored in a dark bottle. The platinum electrode must be heated in a flame prior to each experiment. The lithium chloride solution is prepared by refluxing 200 gm. of the best obtainable grade of the salt with 1 liter of absolute ethyl alcohol; it is stored in a dark bottle in the dark. The reagent used was 0.015 N potassium hydroxide dissolved in absolute ethyl alcohol. It is kept in a blackened Pyrex glass bottle in the dark. Advantageously the bottle is kept rather full to minimize the influence of the oxygen of the air. Daily supplies are withdrawn from this bottle and kept ready for use in a small bottle. The titer of the potassium hydroxide solution was determined by titration of a known aqueous hydrochloric acid solution. The titer should be checked at frequent intervals, as any change in titer indicates a very disturbing change in the solution probably due to spontaneous oxidation. The titrations were carried out with a micrometer microburette of the above mentioned type;<sup>6</sup> a stream of nitrogen bubbles was passed through the solution during the titration to stir the solution and to prevent the interference of carbon dioxide.

The experiments were carried out in 10 ml. of 2.5 per cent collodion solution in a mixture of 50 per cent acetone and 50 per cent absolute ethyl alcohol to which 0.5 ml. of the saturated solution of lithium chloride in alcohol was added. About 20 mg. of quinhydrone were added and nitrogen is bubbled through the solution. The electrodes are inserted into the solution and the potential difference is read on the millivolt scale of the electron tube voltmeter. The reagent is added step-wise and the

<sup>7</sup> Clarke, B. L., Wooten, L. A., and Compton, K. G., *Ind. and Eng. Chem. Analytical Edition* 1931, 3, 321.

<sup>8</sup> Wooten, L. A., and Ruehle, A. E., *Ind. and Eng. Chem. Analytical Edition* 1934, 6, 449.

<sup>9</sup> Ruehle, A. E., *Ind. and Eng. Chem. Analytical Edition* 1938, 10, 130.

<sup>10</sup> For valuable private information we are indebted to Dr. H. M. Spurlin, Hercules Experiment Station, Wilmington, Delaware.



corresponding potential values are determined. The true neutralization point is determined in the conventional graphic manner.

To test the titration method we have carried out some determinations of known concentrations of benzoic and salicylic acid, benzoic acid, undoubtedly, is a weaker acid than the "nitrocellulosic acid" in which we are interested<sup>11</sup>

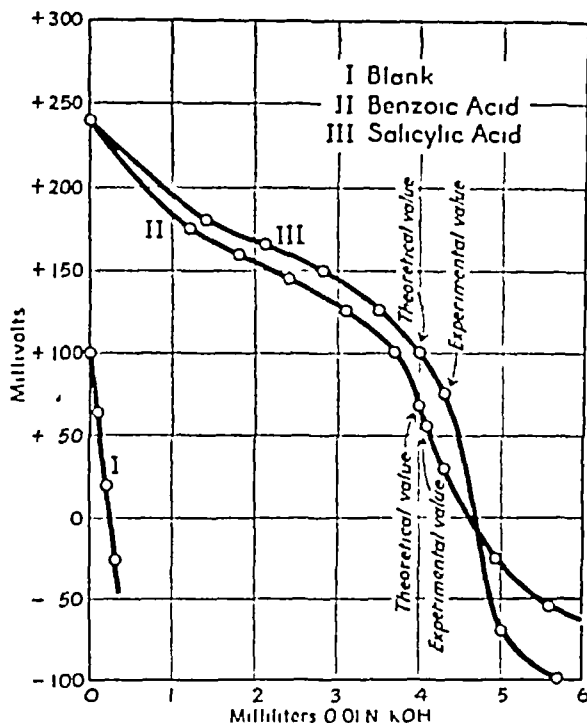


FIG 1

Sample curves for benzoic and salicylic acid are given in Fig 1, together with a blank. The latter, as can be seen easily, is negligible.

Sample curves for the titration of various collodion preparations are given in Fig 2, the ordinate indicates millivolts, the abscissa, milliliters of 0.01 normal solution for 0.25 gm collodion. The shape of the titration curves for collodion does not allow too accurate an evaluation. An error of  $\pm 5$  per cent may occur in many instances. This, however, is of no significance for our particular problem.

Any chemical reaction with the collodion aside from the straightforward

<sup>11</sup> The strength of "cellulosic acid," (oxycellulose) is of the same order of magnitude as salicylic acid. (See, e.g., Neale, S. M., and Stringfellow, W. A., *Tr. Faraday Soc.*, 1937, **33**, 881.) One would expect that "nitrocellulosic acid," oxidized nitrocellulose, would be a stronger acid than non-nitrated oxycellulose.

neutralization of its free acid groups is bound to falsify the results. With a material so liable to be decomposed by alkali solutions as collodion it was therefore necessary to test whether or not the reagent added in the process of titration may not act upon the nitrocellulose. This was the more advisable as conceivably the quinhydrone too could be a disturbing factor.

To decide this question a large sample of a relatively inactive collodion was dissolved in a mixture of 50 per cent acetone and 50 per cent absolute alcohol and titrated with 0.02 N alcoholic potassium hydroxide solution in the presence of the usual con-

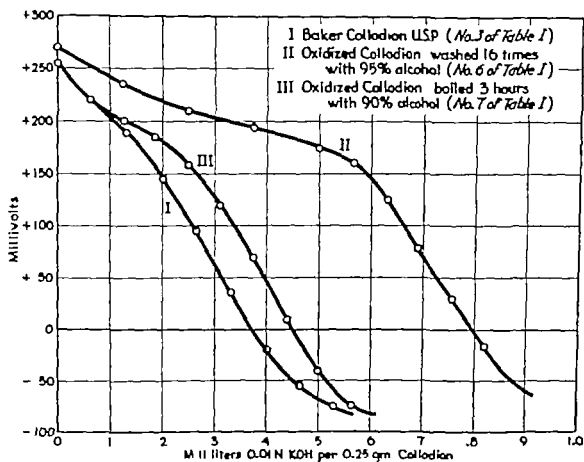


FIG 2

centrations of lithium chloride and quinhydrone. Next the resulting solution was allowed to drip into a great excess of vigorously stirred water, our standard method of preparing fibrous collodion. The fibrous preparation thus obtained was washed and electrodialed for 24 hours to return it to the state of free acidity. After this the material was dried.

A part of the dried product was again dissolved in the standard mixture of alcohol and acetone and titrated as before. The results of the first and this second titration agreed with each other well within limits of experimental error.

The other part of the collodion which had undergone titration, reprecipitation, electrodiaysis, and drying was dissolved in ether-alcohol. Membranes were prepared from this solution and their activity was compared by our usual anomalous osmosis

method<sup>1-4</sup> with the activity of membranes prepared from the original material. No difference between the two preparations could be detected.

From the two foregoing experiments it can be concluded that the collodion in the process of titration does not undergo any chemical changes which influence its acid number. Thus we are sure that the acid number as found by titration of collodion in the dissolved state can be considered to be the correct measure of the free acidity of the collodion.<sup>12</sup>

### III

In Table I are listed the acid values and base exchange data obtained with some representative preparations of different activity and varying acidity.

Column 2 of Table I gives a brief description of the nature of each preparation.

In columns 3 and 4 are listed the ash and  $\text{SO}_4$  contents determined by previously described methods.<sup>2</sup>

Column 5 gives the acid values expressed in milliliters of 0.01 N hydroxide solution per gram of dry collodion, column 6 the acid values corrected for the base content of the ash.<sup>13</sup> Below we will see that for our purpose it is actually

<sup>12</sup> We have also tried the following method to determine the acid number of collodion, it was devised originally by Wilbrandt (Wilbrandt, W., *J. Gen. Physiol.*, 1935, 18, 933) for a similar purpose, though on the basis of entirely different theoretical assumptions, which we have discussed and criticized in an earlier paper (Sollner, K., Abrams, I., and Carr, C. W., *J. Gen. Physiol.*, 1941, 24, 467). The method consists of determining the limiting number of equivalents per gram of collodion of basic material which renders the collodion electroneutral. Dried collodion membranes are prepared from a series of collodion solutions containing increasing concentrations of such basic substances as methylene blue or quinine. The concentration of basic materials is determined at which the concentration potential 0.1 M KCl/0.01 M KCl changes its sign. At this point the negative charges of the membrane are neutralized electrically by what is supposed to be an equivalent quantity of base. For a number of reasons such experiments give results which, though in rough agreement with the results of the titration method, are not better than semiquantitative in character. We therefore only mention this method without going into further details.

<sup>13</sup> The ash content is by no means all basic material, in most cases more than half of the weight of the ash is  $\text{SO}_4$ . In one sample we found 26 per cent  $\text{Al}_2\text{O}_3 + \text{Fe}_2\text{O}_3$ , 7 per cent calcium oxide, and 11 per cent sodium oxide. The aluminum and iron oxides in all probability form but slightly dissociated or non-dissociable compounds. Thus, if we assume that 25 per cent of the weight of the ash behaves like sodium, we certainly have not underestimated the degree to which potentially active acid groups in the collodion are neutralized from the beginning. With an ash content of 0.1 mg per gm collodion this would correspond to 0.025 mg sodium per gm or about 1 milliequivalent of sodium per kilogram dry collodion. Expressed as are the acid num-

immaterial whether we base our considerations on the uncorrected or the corrected acid number values

Column 7 indicates the milliliters of 0.01 *N* hydroxide solution per gram of dry collodion which were used to neutralize 0.5 *N* potassium chloride solution after 48 hours contact with the collodion

Column 8 shows the pH values (as determined with a glass electrode) of the potassium chloride solution after 48 hours contact with collodion.

Column 9 gives the base exchange values calculated from the pH values of column 8 under the assumption that the acidity which is found experimentally is caused by hydrochloric acid in an unbuffered system. The difference between the base exchange values as obtained by direct titration (column 7) and those calculated from the pH values (column 9) is a measure of the dissolution of some material from the collodion which reacts with NaOH. The values of column 9 are therefore a more correct expression of the true base exchange than those of column 7. For a discussion of this point we refer to a prior paper.<sup>4</sup>

Columns 10 and 11 indicate the electrochemical activity of the different collodion preparations. The same method of characterization was used as in preceding papers.<sup>1-4</sup> The membranes tested were approximately of the same porosity as indicated by their behavior when tested with sucrose solution, the figures in column 10 indicating the millimeter pressure rise observed 20 minutes after the membranes filled with 0.25 *M* sucrose solution were placed in distilled water. Column 11 gives the anomalous osmotic rise in millimeters of water obtained after 20 minutes with  $1/512$  potassium sulfate solution. As shown previously,<sup>2, 3</sup> the rate of this rise is a rather sensitive indicator of the electrochemical activity of collodion.

Table II gives some representative data demonstrating the influence of time upon the base exchange. The preparations 3a, 4a, and 6a used for these experiments were not the same but parallel samples of the corresponding preparations Nos. 3, 4, and 6 in Table I.

#### IV

We turn now to the discussion of the main problems of this paper: (a) the comparison of the acid number of preparations of different electrochemical activity, (b) the comparison of the base exchange capacity of the different preparations in the fibrous state, (c) the comparison between the base exchange capacity and the acid number of the individual collodion preparations, and (d)

bers in Table I, this is 0.1 ml. of 0.01 *N* sodium hydroxide solution per gram dry collodion.

In calculating the values of column 6 the appropriate additions have been made to the values in column 5. Since the base content of the ash is probably lower rather than higher than the assumed 25 per cent sodium, some of the corrected values of column 6 are probably slightly too high.

TABLE I  
Acid Number, Base Exchange, and Activity of Various Colloidion Preparations

1	2	3	4	5	6	7	8	9	10	11
	Brand of colloidion and pretreatment (All preparations were precipitated from ether alcohol solutions and dried)	Ash and SO <sub>4</sub> content		Acid No		Base exchange data (48 hrs)			Electrochemical activity	
		Ash per gm dry colloidion	SO <sub>4</sub> per gm dry colloidion	0.01 N KOH per gm dry colloidion		0.01 N NaOH per gm dry colloidion found experimentally on treatment with 0.5 M KCl	pH values found experimentally on treatment with 0.5 M KCl	0.01 N NaOH per gm dry colloidion calculated from pH values of column 8	Osmotic rise with 0.25 M sucrose	Anomalous osmotic rise with $\frac{\mu}{512}$ K <sub>2</sub> SO <sub>4</sub>
				Experimental	Corrected for ash					
		mg	mg	ml	ml	ml		ml	mm	mm
1	Mallinckrodt "Parlodion," commercial preparation	<0.2	<0.1	1.0	1.2	0.011	6.3	0.0016	110 120 127	36 40 45
2	Mallinckrodt "Parlodion," boiled 8 hrs in 90 per cent alcohol (2 alcohol changes)	Very low	Very low	0.85	1.0	0.008	6.4	0.0013	108 110 114	28 18 22
3	Baker Colloidion USSR, commercial preparation	0.4	0.2	1.1	1.5	0.03	5.9	0.004	115 121 130	52 40 60
4	Oxidized colloidion, (Baker Colloidion Cotton, "Pyrocolin") oxidized 48 hrs with 1 M NaOBr and boiled several times with water	0.3	<0.2	3.0	3.3	0.29	4.1	0.26	130 140 158	145 138 178
5	Oxidized colloidion (No 4), washed 8 times with 95 per cent alcohol	<0.3	<0.2	2.7	2.9	0.19	4.5	0.11	135 144 158	180 145 172
6	Oxidized colloidion (No 4), washed 16 times with 95 per cent alcohol	<0.3	<0.2	2.6	2.8	0.03	5.7	0.0066	122 138 148	137 145 155
7	Oxidized colloidion (No 4), boiled 3 hrs with 90 per cent alcohol	<0.3	<0.2	1.4	1.6	0.03	5.7	0.0066	135 140 150	125 134 120

a comparison between the acid number and the base exchange capacity of the various preparations on the one hand and their electrochemical activity on the other

The acid numbers of the different preparations (column 6, Table I) vary only from 1.0 ml. of 0.01 N hydroxide per gm. for the most highly purified preparation to 3.3 ml. for highly oxidized collodion. Only a small fraction of the total acidity can possibly be due to semiesterified sulfuric acid<sup>14</sup>. The ratio of the extremes of the observed acid numbers is only 1:3.3. The mean equivalent weights which correspond to these acid values are 100,000 and 30,000 respectively.<sup>15</sup>

<sup>14</sup> On the basis of more indirect evidence we came in an earlier publication (Sollner K. Abrams, I. and Carr C. W. *J. Gen. Physiol.* 1941 **24**, 467) to the conclusion that the sulfate content plays only a minor rôle if any in determining the electrochemical properties of collodion. This can now be shown definitely by comparing the sulfate contents (column 4 of Table I) with the corresponding acid numbers of column 6. If all the sulfate is present in the semiesterified form, a sulfate content of 0.1 mg. per gm. collodion corresponds fairly accurately to 0.1 ml. 0.01 N hydroxide solution. Thus, with the pure commercial preparations listed in Table I, the possible maximum contribution of sulfuric acid compounds to the overall acidity is only 8 to 13 per cent, with the oxidized collodion preparations less, corresponding to their higher titratable acidity.

<sup>15</sup> The acid numbers of the commercial collodion preparations vary from 1.2 to 1.5 ml. of 0.01 N hydroxide solution per gm. collodion; this corresponds to (mean) equivalent weights of 67,000 to 83,000. We may assume that our collodion corresponds fairly closely to cellulose tetranitrate which carries two  $\text{O}-\text{NO}_2$  groups per glucose residue and has a "molecular weight" of 252. Then, the mean chain length per carboxyl group would be 260 to 330 glucose residues. Using the same technique as with collodion, we found a similar chain length also with several acetylcellulose preparations. Our results are in good agreement with the corresponding values given by different authors for purified cellulose: Heymann and Rabinov (Heymann E. and Rabinov G. *J. Physic. Chem.* 1941 **45**, 1152) e.g. find 300; Sookne and Harris (Sookne A. M. and Harris, M. *J. Research Nat. Bureau Standards* 1940 **25**, 47 (*Nat. Bureau Standards Research Paper RP 1313*)) about 600 glucose residues per carboxyl group. The carboxyl groups are believed to be present as the one end group of the cellulose molecule. (See further e.g. Sookne A. M., Fugitt C. H. and Steinhardt J. *J. Research Nat. Bureau Standards* 1940 **25**, 61 (*Nat. Bureau Standards, Research Paper RP 1314*); Neale, S. M., and Stringfellow W. A. *Tr. Faraday Soc.* 1937 **33**, 881.) We may add that it is customary to assume on the basis of viscosity, osmotic, and ultracentrifuge studies that the degree of polymerization of native cellulose and nitrocellulose derived therefrom is about 2,000 to 3,000 glucose residues per molecule. (See e.g. Ott E. *Ind. and Eng. Chem.* 1940, **32**, 1641.)

From the foregoing figures it is clear that the dissociable acidic groups occupy only a very small fraction of the surface of cellulose and nitrocellulose molecules.

In considering the *base exchange capacity* it is necessary for the reasons outlined above to consider the figures calculated on the basis of pH measurements (column 9). In the following discussion we will assume that the very low base exchange values found with some preparations can be taken at their face value. However, we must recall that these values, as discussed previously at length,<sup>4</sup> are only maximum possible values, the figures given in the table for the cases 1, 2, and 3 are undoubtedly too high. The very great importance of the time factor will be discussed in the next section.

With the base exchange we find enormous differences between different preparations, less than 0.002 ml. of 0.01 N hydroxide solution per gm. for very inactive preparations (compare column 11), values as high as 0.26 ml. for oxidized collodion of high activity, and values down to 0.0066 ml. for oxidized collodion which was treated thoroughly with alcohol, but nevertheless has retained considerable electrochemical activity. The ratio of the lowest and the highest base exchange values reported in Table I is about 1:200, whereas the difference in the acid numbers of the same preparations is as noted above only 1:3.3.

We turn our attention next to the *correlation of acid number and base exchange capacity of the individual collodion preparations*. To do this, we compare the figures of columns 6 and 9 of Table I. This comparison shows that with the pure preparations 1, 2, and 3 not more than one in about 380 to 770 of all the acid groups is available for base exchange. With oxidized collodion, which was purified by repeated boiling with water, No. 4 of Table I, this ratio is about one in 13, with oxidized collodion, which was washed eight times with alcohol (No. 5), the ratio is increased to one in about 26, with more thoroughly purified oxidized collodion, the ratio increases to one in 240 for case 7 and one in 420 for case 6.

Thus we see that there are enormous differences in the availability for base exchange of the acidic groups of the various collodion preparations. The much higher base exchange capacity of oxidized collodion in the fibrous state is not so much due to its higher acid number as to its more open micellar structure. The variations between the several preparations are thus indicative of differences in micellar structure.

The more open structure of oxidized collodion is probably due to the presence of a small percentage of low molecular weight material which inhibits normal formation and arrangement of the micelles. That repelling forces between charged groups—the carboxyl groups—may play an important rôle in the formation of collodion micelles and their arrangement can on the basis of analogous cases be considered to be rather unlikely. The impurities which account for the open structure of oxidized collodion can be gradually removed by purification (cases 5 to 7 of Table I). But even very thorough purification yields a material of a somewhat more open structure (case 7) than the original unoxidized preparation, in spite of the fact that the acid number is reduced approximately to its original value.

We have so far not discussed the time factor with regard to the availability of the acidic groups for base exchange and the typical membrane functions. Our calculations so far have been made on the basis of the base exchange obtained after 48 hours. However we must remember that membranes brought into a KCl solution assume (if they are not unduly thick) their final electrical

TABLE II

*The Influence of the Time of Reaction on the Base Exchange of Various Collodion Preparations*

A. Baker collodion U.S.P. (sample 3a)		
Time of reaction	pH values on treatment with 0.5 M KCl	ME 0.01 N NaOH per gm. dry collodion calculated from pH values
5 min.	—	—
30 min.	6.8	0.0005
1 hr.	6.4	0.0013
6 hrs.	6.2	0.0021
12 hrs.	6.0	0.0033
24 hrs.	5.9	0.0042
48 hrs.	5.9	0.0042
B. Oxidized collodion (sample 4a)		
5 min.	6.0	0.0033
30 min.	5.5	0.011
1 hr.	5.0	0.033
6 hrs.	4.6	0.084
12 hrs.	4.2	0.21
24 hrs.	4.1	0.28
48 hrs.	4.1	0.26
C. Oxidized collodion washed 16 times with 95 per cent alcohol (sample 6a)		
5 min.	6.5	0.0011
30 min.	6.3	0.0017
1 hr.	6.1	0.0026
6 hrs.	5.9	0.0042
12 hrs.	5.8	0.0053
24 hrs.	5.7	0.0066
48 hrs.	5.7	0.0066

properties, i.e. conductance and membrane potential within several minutes as soon as the electrolyte has penetrated. Therefore only those groups which are placed so as to exchange readily can contribute significantly to the characteristic properties of membranes. Though it is impossible to estimate accurately the quantity of these readily exchanging groups, experiments on the influence of time on the base exchange will give some useful hints. As before, we consider the base exchange values which are calculated from the experi-



mental pH values Table II contains such data The preparations used (3a, 4a, 6a) are, as said before, very similar to Nos 3, 4, and 6 respectively in Table I

If we look at the base exchange values obtained after 5 or 30 minutes we certainly obtain a more correct picture of the availability of the dissociable groups which determine the typical electrochemical properties of collodion In addition we must consider the fact that collodion fibers exhibit a greater number of dissociable groups in readily available places than more coherent and compact structures like most collodion membranes, particularly fairly dense ones On this basis we come to the conclusion that the ratio of available dissociable groups in collodion membranes to those present in the preparation is hardly less than fifty times and probably rather a thousand times smaller than given above We may therefore estimate this ratio to be rather 1 500 to 1 1,000,000 than 1 13 to 1 770, according to the preparation used <sup>16</sup>

Finally we turn to the *correlation of acid number and base exchange capacity of the various collodion preparations to their electrochemical activity*

The acid numbers (column 6, Table I) on which we base this comparison do not need any critical remarks For base exchange values we use the data obtained in 48 hour exchange experiments (column 9, Table I), keeping in mind the above discussed restrictions of their significance

As a measure of the electrochemical activity we use the mean of the three values given in column 11 of Table I for each of the collodion preparations It is necessary to recall briefly the basis and significance of these figures <sup>1 2 3</sup> They represent the rate of anomalous osmosis observed under arbitrary but standardized conditions Bag-shaped membranes (30 × 110 mm) of approximately identical porosity (column 10 of Table I) filled with m/512 K<sub>2</sub>SO<sub>4</sub> solution are immersed in water and the pressure rise in a capillary manometer tube is measured after 20 minutes This pressure rise according to experiments by Loeb is for a given membrane proportional to the electrokinetic ( $\zeta$ ) potential times the membrane ( $\epsilon$ ) potential <sup>17</sup> Theoretical considerations of Sollner show that the relationship is more complicated <sup>18</sup> The pressure rise, that is the extent of the anomalous osmosis, is proportional to the electrokinetic ( $\zeta$ ) potential times the difference of the  $\epsilon$ -potentials which arise between different parts or pores of the membrane, this difference is the driving force in the process of anomalous osmosis The  $\zeta$ -potential increases with increasing charge density

<sup>16</sup> These ratios can be taken as a quantitative indication of the discrepancy between collodion membranes and membranes which behave as homogeneous "oil" phases In the latter type of membranes all the functional groups (acid groups in our case) are available for the characteristic membrane function

<sup>17</sup> Loeb, J, *J Gen Physiol*, 1922, 4, 463, and many other papers in the preceding volumes of the same Journal

<sup>18</sup> Sollner, K, *Z Elektrochem*, 1930, 36, 36, 1930, 36, 234

(number of exchanging groups per unit area) up to a certain limiting value which cannot be surpassed. Any further increase of the charge density does not lead to higher values of  $\bar{\epsilon}$ . The correlation of driving force and charge density is not simple, it is not necessarily proportional to the measurable membrane potential. Higher charge density need not necessarily lead to an increase of the difference between local membrane or pore potentials. A simple consideration shows that a positive correlation cannot be expected with high charge densities. Thus the anomalous osmotic pressure rise is by no means a simple and straightforward quantitative measure of the 'electrochemical activity', particularly with highly active preparations.

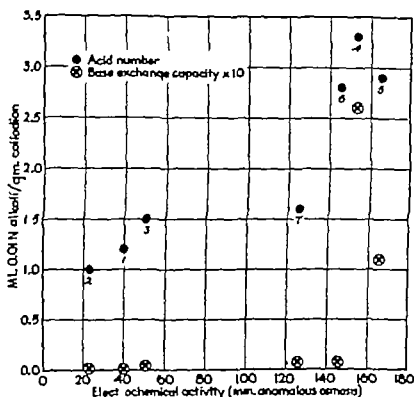


FIG 3

With these reservations in mind we have plotted in Fig. 3 the electrochemical activity of the various preparations given in Table I against their acid numbers (dots) and base exchange capacities (crosses). In order to accommodate both sets of data in one graph the base exchange values are plotted enlarged ten times.

There is a reasonably good correlation between acid number and electrochemical activity. Low acid numbers are found with the preparations of lowest activity; the highest acid numbers are found with the most active preparations, though medium acid numbers are found with a fairly inactive (No. 3) as well as with a fairly active preparation (No. 7). An explanation of this latter discrepancy must be looked for in the above discussed difference in structure between the

commercial (No 3) and the highly purified oxidized preparation (No 7) The base exchange data indicate a somewhat more open structure of the latter material One must assume that this results in a somewhat less smooth, more irregular, and rougher nature of the walls of the pores This would lead to the exposure of a greater number of active groups in spots which can make an essential contribution towards the electrochemical activity

The correlation between base exchange capacity and activity as pointed out in a previous paper is not as good Low base exchange capacity is associated with low as well as with high electrochemical activity, high base exchange capacity is always associated with great electrochemical activity Obviously the base exchange capacity which must be shown by a preparation to give rise to high electrochemical activity is very small, not more than barely measurable, any further increase in base exchange capacity does not cause a great positive increment in the electrochemical activity as measured by the anomalous osmosis method This can be understood on the basis of two factors First, as pointed out before, the electrochemical activity, as measured with the anomalous osmosis method, cannot be expected to increase steadily when the charge density increases over a certain level The second factor must be looked for in this direction the process of anomalous osmosis through the highly porous membranes used takes place essentially in the wider pores which traverse the membrane, it is inconsequential for this process if the functionally active pore walls have a microporous structure If the pore walls have a structure of the latter type, parts of the membrane skeleton, which do not contribute to the process of anomalous osmosis, may easily be available for base exchange Thus the more open microstructure, which as discussed above is found so pronouncedly with the less purified oxidized collodion preparations, easily may account for much of the apparent lack in parallelism between base exchange capacity and electrochemical activity as determined by the anomalous osmosis method If the comparison between electrochemical activity and base exchange were based on short time base exchange values (Table II) a better agreement between the two sets of data would be found, since the differences in base exchange between the different preparations are less pronounced in short time experiments than after 48 hours The inaccuracy of the very low short time base exchange values, however, makes it impractical to evaluate them quantitatively In a forthcoming paper we intend to discuss certain aspects and consequences of the heteroporous character of collodion membranes

One could attempt to use the acidity and base exchange capacity data, which were given above, for some comparison of collodion membranes with monomolecular films or for an estimation of the number of pores per unit area However, we do not think that this at present would be a particularly fruitful beginning The spread of the figures we could start out with is very wide, it also would be necessary to base the calculations on some additional estimates and some arbitrary assumptions The problem of the number of pores per square

centimeter was treated in the past mostly on the basis of the assumption that pores of more or less uniform cross-section traverse the membrane in a fairly regular manner with little or no cross-connections. Such a situation, however, certainly does not prevail in dried collodion membranes or "porous" membranes of the type used in our previous work. We always must remember that the interstices in a collodion membrane are irregular, non uniform, and interconnected, furthermore many dead-end spaces exist undoubtedly.

The availability of the pore space for the most typical membrane function, the penetration of third substances, is moreover not only governed by the complex and unknown interplay of the above mentioned and similar factors but also by the characteristics of the third substance. Pathways which are available for small molecules are unavailable for bigger ones.

In order to characterize structures like membranes with regard to their important functional properties it is necessary to look for new approaches which are less formal than those ordinarily used in the past. A study of the functional properties of the membranes, their permeability, their ionic selectivity,  $\epsilon$  their electromotive properties, and their conductance in solutions of various electrolytes and different concentration will furnish the data of most interest. Knowledge of the geometrical structure of membranes is of interest mainly in as far as it helps to coordinate, to explain, and to visualize the functional membrane properties.

This does not mean that the application of other physical methods in elucidating the structure of collodion membranes is of no interest. Quite to the contrary, we think that such methods should be exploited to the limit, such studies<sup>19</sup> are bound to give us a fuller understanding of the data which may be obtained with the above mentioned methods of functional membrane characterization.

Our next problems will be to prepare fairly uniform membranes with well

<sup>19</sup> Due to the wartime conditions we shall not be able to attack the purely physical aspects of our wider problem in the near future. The obvious approach would be the use of x-rays to obtain some information as to the size and arrangement of the micelles in collodion fibers in porous and in dried membranes. We also think that the electron microscope could conceivably be of great help in the study of extremely thin membranes. If, e.g. the molecules are arranged into micelles in such a manner that many end carboxyl groups come to lie next to each other, like the points of a bundle of pencils, then these groups, if neutralized with ions of a metal having a high atomic number (e.g. Pb or Hg) may become visible with the electron microscope.

Another problem that requires fundamental investigation is the coordination of our findings with regard to the scarcity of dissociable groups in collodion with the conventional concepts of the electric double layer and of the electrokinetic potential. A combination of electroosmotic and cataphoretic studies with collodion should go far towards elucidation of this question. Some of the apparent difficulties will be resolved at least partially by the assumption of structural irregularities which we hope to discuss at greater length in a forthcoming paper.

defined electrochemical characteristics, and to investigate their electrochemical properties,  $\kappa c$ , their conductance and electromotive behavior in solutions of different electrolytes

For much valuable help we are indebted to Dr Charles W Carr

#### SUMMARY

1 The electrochemical behavior ("activity") of collodion membranes depends upon acidic, dissociable groups located in the interstices of the membranes. The active groups can be determined by base exchange measurements. High base exchange capacity is always found with preparations of great "electrochemical activity," medium and low base exchange capacities occur with electrochemically active as well as with inactive preparations. The observed base exchange capacity is determined by two factors: the inherent acidity of the collodion (its mean equivalent weight) and the submicroscopic micellar structure of the collodion. A comparison of the base exchange capacity of various collodion preparations and their inherent acidities therefore allows certain conclusions to be drawn concerning the relative availability of the micellar surfaces in the different preparations.

2 The inherent acidity of various collodion preparations, their "acid number," was determined by electrometric titration. Collodion in the acidic state,  $\kappa c$  after exchange of all other cations for  $H^+$  ions, was titrated in an organic solvent mixture with alcoholic KOH using a quinhydrone electrode. Details of the experimental procedure are given in the paper. The acid numbers, expressed in milliliters of 0.01 N KOH per gram dry collodion, vary from 1.0 for a highly purified collodion preparation of very low electrochemical activity to 3.3 for a highly oxidized sample of very high activity. Acid numbers of about 1.5 (corresponding to an equivalent weight of about 67,000) are found both with inactive commercial and with fairly active oxidized preparations. The base exchange capacity of the same preparations in the fibrous state as measured after 48 hours of exchange time varies from 0.0013 ml 0.01 N NaOH per gm dry collodion for the most inactive preparation up to 0.26 ml 0.01 N NaOH per gm for the most active preparation. Thus the acid numbers over the whole range investigated differ only in the ratio of 1:3.3, whereas the base exchange values differ in the range of 1:200.

3 In the inactive preparation only one in 770 acid groups is available for base exchange, in the most active collodion one group in 13, values between these extremes are found with commercial and alcohol purified oxidized preparations.

4 The high base exchange capacity of the electrochemically active preparations is not so much due to their higher acid number as to their more open structure. This difference in structure is ascribed to the presence of a small

fraction of low molecular weight material which inhibits normal formation and arrangement of the micelles

5 Short time base exchange experiments with fibrous collodion indicate that the number of acid groups available for the typical electrochemical membrane functions may be estimated to be about 50 to 1000 times less numerous than those found in the 48 hour base exchange experiments. It is estimated that in membranes prepared even from the most active collodion not more than one in 500 acid groups may be available for the typical membrane functions, with the less active preparations this ratio is estimated to be as high as one in 1,000,000 or more.



# THE STRUCTURE OF THE COLLODION MEMBRANE AND ITS ELECTRICAL BEHAVIOR

## IX. WATER UPTAKE AND SWELLING OF COLLODION MEMBRANES IN AQUEOUS SOLUTIONS OF ORGANIC ELECTROLYTES AND NON ELECTROLYTES

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### I

In a recent publication Carr and Sollner<sup>1</sup> have reported on the water uptake and the swelling of collodion membranes in water and solutions of strong inorganic electrolytes. They determined the weight and volume changes of collodion membranes when placed in water and when transferred from water to solutions of strong electrolytes. It was found that dried collodion membranes swell reversibly to an appreciable extent when placed in water, the swelling varying from 5 to 11 per cent depending on the brand of collodion. The water uptake as determined by the weight increase is larger than could be accounted for by the volume increase swelling accounting for only 60 to 70 per cent of the water taken up by the membranes. When the "water wetted dried" collodion membranes were transferred from water to solutions of various strong electrolytes, there was no detectable change in volume. Similarly when "porous" membranes were transferred from water to solutions of strong electrolytes, there was no significant volume change.

Without giving further details, Carr and Sollner<sup>1</sup> stated that the problem of water uptake and swelling of collodion membranes is more complex in aqueous solutions of many organic compounds. This is of interest in view of the fact that the permeability of collodion membranes to various organic substances in aqueous solutions was found by several investigators to be anomalously high.

Michaelis and Fujita<sup>2</sup> reported that strychnine, quinine, and other alkaloid cations penetrate dried collodion membranes with approximately the same ease as do sodium ions which undoubtedly are much smaller.

Collander,<sup>3</sup> measuring the relative permeability of about thirty organic non-electrolytes and weakly dissociated compounds mostly acids, found that with a few exceptions the permeability decreased regularly with increasing molecular

<sup>1</sup> Carr C W, and Sollner K. *J Gen Physiol* 1943 27 77

<sup>2</sup> Michaelis, L. and Fujita, A. *Biochem Z.*, Berlin 1925 161 47

<sup>3</sup> Collander R. *Soc Scient Fennica Commentationes Biol*, II. 6, Helsingfors 1926.



size The compounds which in his experiments deviated most strongly from this regular pattern are propionic acid, valeric acid, monochloroacetic acid, phenol, and *m*-nitrophenol It is important to note that a membrane kept for some time in a solution of *m*-nitrophenol was found by Collander to contain much more of the solute than would be expected if its concentration in the water contained within the membrane were the same as in the outside solution Collander links the unusually high permeability of the *m*-nitrophenol with this effect

Hober<sup>4</sup> determined the relative permeability through positive membranes of a number of organic and inorganic anions in solutions of their Na salts For this purpose he used collodion membranes impregnated with a basic dye-stuff It would be premature to discuss Hober's very interesting results in detail here It must suffice to state that in many cases the permeability of the organic anions is much higher than the permeability of inorganic anions of smaller molecular size *Eg*, the fatty acid ions from acetate to the valerate ion possess permeabilities comparable to that of the much smaller chloride ion, and the fatty acid anions above valeric acid have even greater permeabilities This behavior Hober attributes to the surface activity of the organic ions which are believed to be concentrated on the pore walls, and thus to move faster across the membrane

In view of the fact that air-dried collodion membranes swell in water,<sup>1</sup> it seemed advisable to investigate whether the solutions of the substances that were found to exhibit anomalous permeabilities might have a specific swelling effect The detection of such an effect, of course, would be most important in determining the limits of applicability of collodion membranes to permeability studies, in addition it would cast light on the findings of the above mentioned investigators We therefore have investigated the swelling of collodion membranes in aqueous solutions of some organic substances and the uptake of solute from these solutions by the membranes

The organic substances for this investigation were chosen preferentially from three classes of compounds One group was selected from among those weakly or non-dissociated substances used by Collander which would be most likely to influence the swelling of collodion, such as fatty acids, phenol, and nitrophenol, secondly, some definitely hydrophilic compounds such as glycerine, glucose, and citric acid, and thirdly some strong organic acids, sulfonic acids, were tested, the sodium salts of which were found by Hober to behave very anomalously

This study has been confined to dried collodion membranes since any specific swelling effect that may be found with dried collodion membranes would also result in a change of structure of "porous" membranes

<sup>4</sup> Hober, R., *J Cell and Comp Physiol*, 1936, 7, 367

## II

The experimental procedure is briefly as follows: flat dried collodion membranes were prepared, their weights determined, and their volumes ascertained with a pycnometer filled with mercury; they then were placed into the solutions of the various organic compounds. After measured duration of immersion in the solutions, the membranes were removed, blotted, and their weights and volumes again determined. Finally, in a number of representative cases the amount of solute contained in the membranes at equilibrium with various solutions was determined.

The technique of the weight and volume measurements was the same as used by Carr and Sollner which was described in another paper.<sup>1</sup>

In some cases the weight and volume measurements were made at relatively frequent intervals in order to ascertain the swelling of the membranes as a function of the time. In all cases enough determinations were made to assure that equilibrium values of weight and volume had been reached. The material used throughout this investigation was Baker U.S.P. collodion.

To determine the amount of organic solute contained in the membranes the following procedure was used: the membrane was removed from the solution and momentarily dipped into distilled water; then it was placed into a 150 × 15 mm. test tube containing ca. 10 ml. of distilled water which covered it completely. After a sufficient amount of the organic substance had diffused out of the membrane in most cases after a few days, the membrane was removed from the solution and the latter was titrated. The membrane was placed again in distilled water and the resulting solution was titrated as before after several days. This procedure was repeated until successive titrations yielded zero values. A membrane which was free of organic solute was used as a control and titrated along with the others. With the acids the titration was carried out with 0.02 N NaOH, using a syringe micro buret which allowed readings to 0.002 ml. The total amount of reagent required for the control was subtracted from the amount required for the titration of the membranes. The phenol solutions were titrated in a similar manner with 0.1 N solution of KBr-KBrO<sub>3</sub>. In all cases the analyses were carried out after swelling equilibrium had been established.

The results of the weight and volume measurements are given—as by Carr and Sollner—as milligrams and cubic millimeters weight and volume increase respectively per cubic centimeter of dry membrane which occur when dry collodion membranes are immersed in the various solutions.

The accumulation of solute by the membranes was calculated as follows: the amount of substance actually present in a membrane was divided by the quantity that would be present if the concentration of the solute in the solution which is contained within the membrane were the same as in the bulk of the

solution. This ratio obviously is a quantitative measure of the relative accumulation of solute within the membrane.

The quantity of solute present in the membrane is found by analysis. The quantity of solute that would have entered the membrane if the measurable weight increase were caused by the uptake of unchanged solution can readily be calculated from the weight increase and the known specific gravity and the concentration of the solution. The former quantity divided by the latter gives the desired ratio which we call the "accumulation factor."

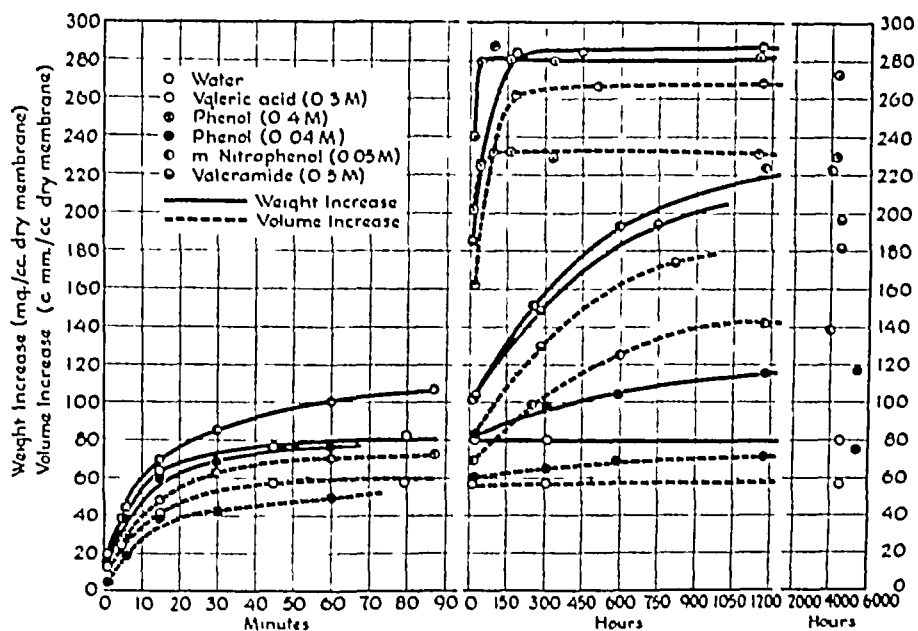


FIG 1

It is of interest to compare the quantity of solute contained in the membrane with the corresponding weight or volume increases. The clearest picture of this relationship is obtained by comparing the quantity of solute taken up per cubic centimeter of dry membrane with the corresponding "characteristic additional weight increase." This latter quantity we define as the weight increase in solution minus the weight increase in water per cubic centimeter of dry collodion.

### III

Fig 1 gives the relative volume and weight increases of dried collodion membranes in aqueous solutions of several organic compounds as a function of time. The equilibrium values of the weight and volume increases per cubic centimeter

TABLE I

*The Interaction of Dried Collodion Membranes with Aqueous Solutions of Various Organic Compounds*

1	2	3	4	5	6	7
Solute	Concentration of solution	Weight increase per cc. dry membrane	Volume increase per cc. dry membrane	"Accumulation factor"	Uptake of solute per cc. dry membrane	"Characteristic additional weight increase per cc. dry membrane"
	<i>moles/liter</i>	<i>mg</i>	<i>c.mm</i>		<i>mg</i>	<i>mg</i>
Water	—	80	57	—	—	—
Acetic acid	0.54*	97	72	8.7	25.4	17
Propionic acid	0.52*	114	90	13.0	52.9	34
Butyric acid	0.28*	125	101	22.7	67.8	45
Butyric acid	0.49*	161	137	15.6	108	81
Valeric acid	0.26*	276	260	32.1	232	196
Monochloroacetic acid	0.53*	152	103	9.3	67.8	72
Ethyl alcohol	0.5	83	57	§	§	3
Isobutyl alcohol	0.5	122	108	§	§	42
Isamyl alcohol	0.5	136	127	§	§	56
Formamide	0.5	85	66	§	§	5
Valeramide	0.5	196	181	§	§	116
Phenol	0.042*	117	76	114	47.4	37
Phenol	0.38*	282	232	20.8	234	202
m-Nitrophenol	0.05	224	145	§	§	144
Benzene sulfonic acid	0.5	75	56	0.00	0.0	-5
β-Naphthalene sulfonic acid	0.5	78	57	0.00	0.0	-2
Glycerine	0.5	96‡	72‡	§	§	6
Glucose	0.5	82‡	70‡	§	§	-8
Citric acid	0.5	99‡	75‡	0.00	0.0	9

\* Concentration determined analytically after establishment of swelling equilibrium.

‡ These membranes were cast at a later date—the weight and volume increases in water for the membranes in this group are 90 mg per cc. dry membrane, and 70 c.mm per cc. dry membrane respectively.

§ Not analyzed.

of dry membrane for all the substances tested are summarized in columns 3 and 4 of Table I. The "accumulation factors" for several solutes are given in column 5; the solute uptake in milligrams per cubic centimeter of dry mem-

brane and the "characteristic additional weight increase" in milligrams per cubic centimeter of dry membrane are shown in columns 6 and 7

## IV

The data presented in columns 3 and 4 of Table I show that the dried collo-dion membrane exhibits widely different behavior when placed in solutions of various organic compounds, the weight and volume increases of the membrane differ greatly with the nature and concentration of the solute, being in many cases far larger than in water

No significant specific swelling effect is observed with the 0.5 M solutions of ethyl alcohol, benzene sulfonic acid,  $\beta$ -naphthalene sulfonic acid, glycerine, glucose, and citric acid. The weight and volume increases are significantly larger than in water alone with acetic acid and the higher fatty acids, monochloroacetic acid, isobutyl and isoamyl alcohol, valeramide, phenol, and *m*-nitrophenol. With formamide the results seem to be ambiguous. In the homologous series of the fatty acids, alcohols, and amides the swelling effect increases with increasing molecular weight. In view of this, one may be inclined to think that a real though small specific swelling effect exists in the case of the formamide solution. The swelling action of a solute is greater, the higher its concentration.

Fig. 1 shows for a few representative cases that the rate at which swelling equilibrium is attained differs markedly for the various solutions. When a dried membrane (prepared from Baker collodion USP) of about 0.15 mm thickness is placed in water, swelling equilibrium is reached in approximately 80 minutes, a similar behavior is observed in the case of the solutions of those substances which do not show any specific swelling effect. With solutions which show a pronounced swelling effect this time varies from about 100 hours for 0.26 M valeric acid and 0.38 M phenol to about 1000 hours with 0.042 M phenol and 0.05 M *m*-nitrophenol solutions.

From the data of column 5 it is seen that the relative accumulation of the organic solute within the membrane, expressed by the "accumulation factor," differs very widely with the various solutes. In the two instances in which two concentrations of the same solute were tested the "accumulation factor" is higher with the more dilute solution.

A comparison of columns 3 and 4 with column 5 shows a very marked parallelism between the swelling caused by a solute and its tendency to accumulate within the membrane, the compounds which cause the most pronounced swelling are also accumulated most strongly. The increase in the "accumulation factor" with increasing molecular weight in the homologous series of the fatty acids may be specially mentioned. The substances which do not show any specific swelling effect show "accumulation factors" smaller than one, this means that the water in the membrane contains less of the solute than it does

in the surrounding solution. Three of the organic substances tested, benzene sulfonic acid,  $\beta$ -naphthalene sulfonic acid, and citric acid are actually excluded completely from the membranes.<sup>5</sup>

To use conventional terminology, one may say that typical "hydrophilic" substances have little influence on the swelling of collodion membranes and are not accumulated in them, whereas "carbophilic" substances make the membranes swell and are accumulated.

The characteristic swelling which is observed with some solutes is entirely due to the accumulation of a corresponding quantity of the solute within the membrane, as can be seen from a comparison of columns 6 and 7. The absolute uptake of solute per gram of dry membrane (column 6) is at least as great as the 'characteristic additional weight increase' per gram of dry membrane in the same solutions (column 7), with some solutes it seems to be significantly greater. The water content of the membranes in equilibrium with the solutions is therefore scarcely as high in some cases probably significantly lower than in pure water.<sup>6</sup> A collodion membrane which has taken up a significant quantity of organic solute must be considered as a structure substantially different from a similar membrane wetted with water.

A pronounced parallelism is apparent between the anomalously high permeabilities described by Collander with certain compounds and their accumulation and the swelling effect caused by their solutions. All the compounds Collander found to deviate from the expected permeability—phenol, *m*-nitrophenol, propionic acid, monochloroacetic acid, and valeric acid—exhibit a pronounced swelling effect and are accumulated in the membranes. Substances which in our experiments do not show a specific swelling effect and are not accumulated—or which on the basis of their structure must be expected to act so—show normal permeability characteristics according to their molecular size.<sup>7</sup>

<sup>5</sup> The accumulation factor was also determined for two inorganic electrolytes. HCl and HNO<sub>3</sub> both show an accumulation factor smaller than 1.003 in the case of HCl and 0.78 in the case of HNO<sub>3</sub>. It is of interest to note that HNO<sub>3</sub>, which, as shown by Collander,<sup>2</sup> penetrates collodion much faster than does HCl, shows a much higher accumulation factor than the latter. Nitric acid is known to have a strong affinity to cellulose, forming at higher concentrations a definite molecular compound (Knecht's compound).

<sup>6</sup> The unusually large differences between the figures for the weight and volume increases in the cases of monochloroacetic acid, phenol, and nitrophenol are of course due to the high specific gravities (1.58, 1.07, and 1.48 respectively) of these substances. The converse holds true for the unusually small differences between the values for weight and volume increase found with valeric acid (sp. gr. 0.94) and isoamyl alcohol (sp. gr. 0.81).

<sup>7</sup> Collander did not test the sulfonic acids. No data seem to be available on their permeability through collodion membranes.

With positive, dyestuff-impregnated collodion membranes the parallelism between anomalous permeability and accumulation is not complete. The unusually high permeability of fatty acid ions in neutral solution is paralleled by the swelling effect and the accumulation of the free acids. The same is not true, however, for the high permeability of aromatic sulfonic acid anions in neutral solution. This discrepancy is hardly surprising in view of the different conditions in Hober's permeability and our swelling and accumulation studies with negative membranes.

On the basis of available information it is impossible to discuss in a satisfactory manner the molecular mechanisms causing the accumulation and the swelling effects and the correlated increase in permeability. The situation is undoubtedly fairly complex. Accumulation can result from adsorption on the micellar surfaces, from filling of intermicellar spaces, and from an absorption of the solute by the micelles. Roughly corresponding to these three degrees of interaction between solute and membrane one would expect little or no specific swelling, moderate specific swelling, and strong specific swelling which in its highest degree approaches dissolution.

These processes obviously are not independent of each other, the observed effects depend upon the nature of the solute and its concentration as well as of the time of interaction between solution and membrane. At low concentrations surface adsorption must be favored over absorption in the interior of the collodion micelles. In a similar manner the alkali salts of organic acids may be strongly adsorbed, but they hardly would dissolve in the mass of the collodion, though the weakly dissociated free acids, which are essentially non-electrolytes, may readily do so.

That the permeability of the accumulated solutes is greater than can be expected on the basis of their molecular size undoubtedly can be due to several different mechanisms. There is first the possibility that a solute which is concentrated in the adsorption layer on the micellar surfaces migrates in the adsorbed state,<sup>8</sup> as suggested by Sollner<sup>9</sup> and Hober.<sup>4</sup> If the adsorption is more pronounced, liquid layers of the solute wetting the membrane may result which, stretching continuously between the two sides of the membrane, could easily account for an increased rate of penetration of the solute. If the micelles absorb and dissolve the solute there is further the possibility that some of the solute diffuses through the swelled collodion micelles themselves. Swelling, furthermore, is bound to result in some change in the pore structure of the membrane which may also lead to an increased rate of permeation of the solute. That the time factor too must be considered is obvious. Adsorption is a fast process and its consequences therefore must be apparent in short time experi-

<sup>8</sup> Volmer, M., and Estermann, I., *Z. Physik*, 1921, 7, 13. Volmer, M., and Adhikari, G., *Z. Physik*, 1925, 35, 170.

<sup>9</sup> Sollner, K., *Kolloid-Z.*, 1933, 62, 31.

ments, absorption and dissolution are relatively slow processes, their full effect is only felt after prolonged contact between solution and membrane

From the foregoing discussion it is clear that swelling, accumulation, and anomalous permeability need not necessarily be parallel in all cases. One can readily conceive of instances in which accumulation without swelling may cause an increased permeability<sup>10</sup>

The interaction of a first solute with the membrane must affect the permeability to second solutes. Blocking of some pathways by the first solute,<sup>11</sup> changes in the geometrical and electrical structure of the membrane, and interaction between the second solute and the first which is present locally in high concentration, as well as other effects, can occur depending on the nature and concentration of the solutes. This makes general predictions hazardous. Careful experimental investigation alone can clarify this problem.

Further discussion seems superfluous since the purpose of the present investigation is only to demarcate the approximate limits of the usefulness of the collodion membrane as a general model of the non-swelling, inert, porous membrane.

Collodion membranes seemingly act as inert membranes with the aqueous solutions of the strong, weakly adsorbable<sup>12</sup> electrolytes and those typically hydrophilic organic substances which are reasonably free from carbophilic groups. With all other substances the situation needs careful individual examination.

The instances of a specific interaction between organic solutes and collodion membranes are apparently much more numerous than has previously been assumed. The anomalies of permeability resulting from this interaction which were observed in the past with certain carbophilic compounds are now more clearly understood as a result of the specific interaction of solute and membrane.

In future work it therefore will be necessary to ascertain the extent of a possible interaction between any given solute and the membrane. A sharp distinction must be made between phenomena which are characteristic for porous membranes in general and observations which are due to a specific interaction between solute and membrane.

The use of membranes prepared from other material than collodion, e.g., dehydrated collodion (cellulose) or various silicates obviously will be helpful.

<sup>10</sup> Membranes of porous character have interstices of a whole spectrum of sizes. If on account of its molecular size the solute cannot enter the smaller pores but may enter the bigger ones and be adsorbed there then it is possible that in spite of an overall 'accumulation factor' smaller than 1 an abnormally high permeability due to adsorption may be found.

<sup>11</sup> Weech, A. A. and Michaels, L. *J. Gen. Physiol.*, 1928 12 55

<sup>12</sup> Nitric acid according to the results of Collander and ourselves cannot be included in this group.



in clarifying the question of the effects of a specific solute-membrane interaction

The interaction between solute and membrane is, of course, a phenomenon of considerable interest in its own right, primarily since such interaction undoubtedly plays an important rôle in living membranes. For an investigation of this problem, however, it may be advisable to use membranes more readily comparable to living tissues than collodion.

#### SUMMARY

1 Dried collodion membranes are known to swell in water and to the same limited extent also in solutions of strong inorganic electrolytes (Carr and Sollner). The present investigation shows that in solutions of organic electrolytes and non-electrolytes, the swelling of dried collodion membranes is not as uniform, but depends on the nature of the solute.

2 The solutions of typically "hydrophilic" substances, *e g*, glycerine, glucose, and citric acid, swell collodion membranes only to the same extent as water and solutions of strong electrolytes.

In solutions of typically carbophilic substances (*e g*, butyric acid, valeric acid, isobutyl alcohol, valeramide, phenol, and *m*-nitrophenol) the swelling of the membranes is much stronger than in water, according to the concentration used. For the brand of collodion used the swelling in 0.5 M solution was in some cases as high as 26 per cent of the original volume, as compared to 6 to 7 per cent in water. Therefore, in these solutions the "water-wetted dried" collodion membrane is not rigid, inert, and non-swelling, but behaves as a swelling membrane.

3 The solutes which cause an increased swelling of the membranes are accumulated in the latter, the degree of accumulation being markedly parallel with the degree of their specific swelling action.

4 The anomalously high permeabilities of certain carbophilic organic solutes reported by Michaelis, Collander, and Hober find an explanation in the specific interaction of these substances with collodion.

5 The use of the collodion membrane as a model of the ideal porous membrane is restricted to those instances in which no specific interaction occurs between the solute and the collodion.

# THE EFFECT OF URETHANE ON THE CONSUMPTION OF OXYGEN AND THE RATE OF CELL DIVISION IN THE CILIATE *TETRAHYMENA GELEII*

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## INTRODUCTION

The effects of narcotics on several types of cell including yeast, luminous bacteria, and brain cortex have suggested to us (Fisher and Stern 1942) that the normal oxygen consumption of those cells may be due to two or three parallel chains of oxygen-consuming reactions. It was shown in yeast that normal cell division appears to depend upon the operation of a specific one of these fractions of the total oxygen consumption of the cell. Implications having a possible general interest arise from this interpretation of the effects of narcotics (Fisher, 1942). It is consequently desirable that its validity be thoroughly explored.

Within the past few years the conditions necessary to maintain bacteria free cultures of many protozoa have been determined. It is therefore feasible to study the relation between cell respiration and cell division in these cells in the manner applied to yeast. Experiments have now been made for this purpose on the ciliate, *Tetrahymena geleii* (Ferguson 1940) as many of the conditions and characteristics of growth in it are known and since it was already being maintained in pure culture for other purposes by one of us (Ormsbee 1942). Specifically, the effects have been determined of a series of concentrations of ethyl carbamate (urethane) on the rate of cell division and on the rate of oxygen consumption in that organism.

## Material and Methods

The Hetherington strain of the ciliate *Tetrahymena geleii* was used in the experiments to be reported. The cultures were grown in 250 ml flasks of the type described by Kidder (1941). Each flask contained 100 ml. of the medium a 2 per cent solution of Difco proteose peptone in redistilled water prepared in a Pyrex still. The methods of making sterility checks and population counts are described by Ormsbee (1942). To determine the effect of urethane on growth, various quantities of this substance in solution (sterilized by Seitz filtration) were added to the cultures after these had reached the exponential phase of growth.

The organisms used for the respiratory measurements were taken from flasks for which the population curve was determined as growth proceeded. Experiments were made on cells from cultures in the exponential phase of growth as well as from cul-

## SUMMARY

To my reading, therefore, this interest in the psychology of the tuberculous is evidence of the wish of our profession to return to the study of man in his wholeness as he was seen by the early Christian physician, and was treated in the first hospitals of the Christian Church. The priest and the doctor long ago took separate roads in their approach to the complete man, the priest concentrating on the soul, the doctor on the body, each more and more jealously retaining his part of the whole, and only seldom meeting on what has now been recognized as common ground for both, the mind of man, through which he translates his spiritual experiences and his bodily reactions. I believe the conjunction of their forces holds great promise for the future, it will avoid for both the dangers of unscientific quackery and the mass hysteria of bogus "spiritual healing", and make possible a further and welcome advance in the field of preventive medicine.

## RESUMEN

De acuerdo con mi información, este interés en la psicología del tuberculoso es una evidencia del deseo de nuestra profesión de volver al estudio integral del hombre tal como fué considerado por el médico cristiano primitivo y como fué tratado en los primeros hospitales de la Religión Cristiana. El sacerdote y el médico hace mucho tiempo que siguieron caminos separados en su relación con el hombre completo, el sacerdote dedicándose al alma y el médico al cuerpo, y cada uno de los dos reteniendo celosamente su parte del todo sólo una vez,—reuniéndose en lo que ahora se ha reconocido como la base para ambos, la mente humana, a través de la cual el hombre traduce su experiencia espiritual y sus reacciones corporales.

Creo que la conjunción de la fuerza de ambos, mantiene una gran promesa para el futuro, para ambos evitará los peligros de el charlatanismo anticientífico de la histeria de masas de la llamada "curación espiritual," y aún hacer posible un avance deseable en el campo de la medicina preventiva.

## RESUME

L'intérêt qui se manifeste maintenant pour la connaissance de la psychologie du tuberculeux révèle le désir que l'on a, dans notre profession, de revenir à l'étude de l'homme tel que l'envisageait le médecin des premiers temps du Christianisme, et tel qu'on le traitait dans les premiers hospices religieux de la chrétienté.

Il y a longtemps que le prêtre et le médecin ont pris des chemins séparés pour étudier l'homme, le prêtre s'attachant à l'âme et le médecin au corps. Ils gardaient chacun jalousement leur domaine, ne se rencontrant que rarement sur le terrain qui a été maintenant reconnu commun pour l'un et l'autre, l'intelligence de l'homme, grâce à laquelle il traduit à la fois ses expériences spirituelles et ses réactions corporelles.

L'auteur pense fermement que l'union de ces deux éléments sera très fructueuse pour l'avenir. Ainsi pourra être évité pour tous les deux le danger d'un charlatanisme contraire à la science et de l'hystérie collective d'une fausse guérison par l'esprit. Ainsi sera réalisé un heureux progrès dans le champ de la médecine préventive.

# Nisentil\* As an Analgesic in Bronchoscopy

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A satisfactory bronchoscopic procedure under local anesthesia requires adequate sedation to allay apprehension and effective analgesia to permit manipulation of the bronchoscope. Barbiturates administered prior to the instillation of a local anesthetic usually provide sufficient sedation and have been adopted as a routine by many. The list of analgesics used in bronchoscopy is on the other hand long and varied, and is constantly being revised as new agents are introduced. It was in this connection that alphaprodine (Nisentil\*) was subjected to clinical trial in the bronchoscopy clinic of the Tuberculosis Service, Los Angeles County General Hospital.

Alphaprodine is a synthetic analgesic piperidine derivative first reported by Ziering and Lee<sup>1</sup> in 1947. The satisfactory effect of this drug in relieving pain in patients with inoperable cancer was reported by Houde, Rasmussen and La Due<sup>2</sup>. It was also used by Smith and Nagyfy<sup>3</sup> in obstetrical cases with good analgesic effect. These observers also noted that repeated administration of the drug was possible because of its short duration of action. Kane<sup>4</sup> administered it to 1000 obstetrical cases and obtained satisfactory analgesia in 98.1 per cent of the deliveries.

## *Material and Method*

This report presents the results obtained with alphaprodine in 119 consecutive bronchoscopies. Local anesthesia and analgesia were customarily induced as follows. One hour prior to bronchoscopy a barbiturate was given orally. Topical anesthesia was induced by gargling with 5 cc of a 1/4 per cent pontocaine solution, and the instillation of 8 cc of a 1/2 per cent solution of pontocaine into the larynx over a period of 15 minutes. Nisentil was then administered subcutaneously 15 minutes before bronchoscopy, since full effect of its analgesic action was customarily obtained within that time. The dosage of the analgesic and that of the pre-anesthetic barbiturate, sodium pentobarbital, is shown in Table I.

TABLE I  
*Dosage*

Cases	Nisentil	Sodium Pentobarbital
16	15 mg	3 grains
98	30 mg	1½ grains
5	60 mg	3 grains

\*Supplied by Hoffmann-La Roche Inc, Nutley, N J

\*\*From the Tuberculosis Service, Los Angeles County General Hospital

The age of the patients in this series varied widely, a majority being more than 50 years old. The clinical diagnoses and indications for bronchoscopy were rather diverse and are given in Table II.

TABLE II  
*Diagnoses or Indications for Bronchoscopy*

Bronchial tuberculosis	18
Broncho-pulmonary suppurative disease	22
Bronchogenic neoplasm	13
Pulmonary hemorrhage	2
Non-specific bronchitis	3
Negative endobronchial tree	51
Biopsies	13
Bronchial dilation	7

### *Results*

The analgesic effect was graded good, fair or poor by the bronchoscopist immediately following the procedure (See Table III).

TABLE III  
*Analgesic Effect*

Nisentil (Subcutaneous)	Sodium Pentobarbital (Oral)	Number of cases	Good	Fair	Poor
15 mg	3 grains	16	3	13	0
30 mg	1½ grains	98	95	0	3
60 mg	3 grains	5	4	0	1

The analgesia produced by 15 mg of alphaprodine and 3 grains of sodium pentobarbital was considered fair, while that obtained with 30 mg of the analgesic and 1½ grains of sodium pentobarbital was rated as good, (50 of the 98 cases had a satisfactory analgesic effect). Of the five cases that received 60 mg of alphaprodine and 3 grains of sodium pentobarbital, four had a good analgesic effect, but two patients in this last group exhibited undesirable side effects manifested by apnea and cyanosis which was relieved by the administration of oxygen and respiratory stimulants. Both of these patients were more than 60 years of age and were apparently over medicated by the combination of 3 grains of sodium pentobarbital and 60 mg of the narcotic. When overdosage was avoided the only side effects noted were those of dizziness and nausea in about 10 per cent of patients. These were mild and transitory, and did not require treatment.

The suppressive effect of alphaprodine on the cough reflex was not evaluated in this study. The observation volunteered by our head nurse in charge of the bronchoscopy clinic, does however appear worthy of mention. She notes that coughing during and immediately following bronchoscopy is much reduced since alphaprodine has replaced morphine and demerol as the analgesic. Investigation of this property of alphaprodine seems desirable.

### *Discussion*

Among the requisites of an ideal analgesic for bronchoscopy one might include the following

- (a) Rapid induction
- (b) Effective relief of pain
- (c) Non-interference with the patient's ability to cooperate during the procedure
- (d) A total duration of action not significantly longer than that of bronchoscopy
- (e) A minimum of side and after effects

Alphaprodine has an induction time of 10 to 15 minutes, it proved an effective analgesic agent in 96 per cent of the 119 bronchoscopies in this series, it did not interfere with the patient's ability to cooperate, its duration of action was approximately 2 hours, its side effects were limited to a mild transient dizziness occurring in about 10 per cent of the patients, and it left no after effects. It would appear therefore that this synthetic narcotic is certainly worthy of consideration as an analgesic in bronchoscopy.

Of the dosage schedules employed, 30 mg of alphaprodine preceded by  $1\frac{1}{2}$  grains of sodium pentobarbital gave the best results. Admittedly this may not be the optimal routine dosage. Other dosage schedules are being considered but have not as yet been evaluated. The use of 60 mg of the narcotic and 3 grains of sodium pentobarbital may result in pronounced respiratory depression, particularly in older patients.

### SUMMARY

1 Alphaprodine was used in 119 bronchoscopies with satisfactory analgesia in 96.6 per cent.

2 Best results were obtained with 30 mg of the narcotic injected subcutaneously, preceded by sodium pentobarbital,  $1\frac{1}{2}$  grains, orally.

3 Side effects were minimal, consisting of mild, transient dizziness and/or nausea, occurring 10 or 15 minutes after administration and clearing spontaneously in a few minutes. The retching and/or vomiting encountered with morphine and some synthetic narcotics were singularly absent.

4 When alphaprodine and a barbiturate are used in conjunction a synergistic depression of respiration results.

5 This drug appears to be an acceptable analgesic agent for bronchoscopy. It provides prompt and effective analgesia, has a short duration of action, and leaves a clear sensorium.

### RESUMEN

1 Se usó la Alfaprodina en 119 broncoscopías y se obtuvo analgesia satisfactoria en el 96.6 por ciento.

2. Los mejores resultados se obtuvieron con 30 miligramos del narcótico inyectados subcutáneamente precedidos de uno y medio granos de pentobarbital sódico, por vía oral

3 Los efectos colaterales fueron mínimos consistentes en moderada sensación de mareo y/o náusea después de 10 o 15 minutos de la administración, lo que desapareció espontáneamente en pocos minutos

4. Cuando se administran la alfaprodina y un barbitúrico conjuntamente, resulta una sinérgica depresión de la respiración

5 Parece que esta droga es un analgésico aceptable para la broncoscopia Proporciona pronta y efectiva analgesia, tiene corta duración de acción y no afecta el sensorio

### RESUME

1 L'auteur a été très satisfait de l'analgésie obtenue par l'alphaprodine dans 96,5% des 119 bronchoscopies qu'il a pratiquées à l'aide de ce produit

2 Les meilleurs résultats furent obtenus par injections sous-cutanées de 30 mmgr du produit précédées par l'administration par voie buccale de pentobarbital de soude

3 Les effets secondaires se montrèrent négligeables Ils consistèrent en vertiges légers et transitoires, et en un état nauséux, associé ou non à ces vertiges, survenant dix à quinze minutes après l'injection, et disparaissant spontanément en quelques minutes Les nausées et vomissements auxquels on est exposé lorsqu'on utilise la morphine ou certains anesthésiques synthétiques ont manqué totalement avec ce procédé

4. Quand l'alphaprodine et un barbiturique sont utilisés simultanément, il en résulte une dépression respiratoire

5 Ce produit semble être un analgésique très bien adapté à la bronchoscopie Il détermine une insensibilité rapide et réelle a une action de durée très limitée, et laisse à sa suite un état psychique intact

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# The Effects of Pulmonary Infection on Cardiorespiratory Functions in Chronic Emphysema.\*

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Investigations of cardiorespiratory functions in pulmonary diseases have in recent years contributed much to the understanding of the development of pulmonary heart disease. Harvey et al<sup>1</sup> in a recent publication have stressed the importance of anoxia in patients with chronic pulmonary emphysema as a cause for the deterioration of heart function. According to them, acute anoxia may precipitate the development of congestive heart failure and the relief of anoxia may bring about marked improvement in cardiac function. The main causes of acute anoxia may be bronchial obstruction and acute pulmonary infection.

Two cases of emphysema were recently observed in which the development of acute pulmonary infection and anoxia was associated with congestive heart failure. Recovery from the infection and anoxia was accompanied by regression of the signs of congestive heart failure. In one case, also, the interesting effects of treatment with adrenocorticotrophic hormone on pulmonary functions in the different stages of pulmonary emphysema were recorded.

## Methods

**Pulmonary function tests.** Lung volumes and maximum breathing capacity were measured by the spirographic technique<sup>2</sup>. All the data were calculated to 37° C, saturated and prevailing barometric pressure. The predicted vital capacity and maximum breathing capacity were calculated by the formulas of Baldwin et al<sup>3</sup>. Arterial blood gases were determined by the method of Van Slyke and Neill<sup>4</sup>. Blood was obtained from the brachial artery using an indwelling Cournand-type needle. The blood was collected by the technique of Riley et al<sup>5</sup> using heparin to prevent clotting and a small globule of mercury in the syringe for proper mixing. Exercise tests on the Master two-step stairs were performed during three minutes<sup>6</sup>. 100 per cent oxygen breathing was maintained for three minutes. Venous pressure was measured by the direct Moritz and Tabor method. Circulation time was determined with decholin. ACTH was given by intravenous drip infusion of small doses<sup>7, 8</sup>.

*Case 1.* Z. M., a 45 year old male was admitted to the hospital on May 25th, 1952, for the fifth time. The chief complaints were fever, cough and shortness of breath. His past history revealed that for many years he had suffered from attacks of respiratory infections and bronchial asthma. A diagnosis of obstructive emphysema and spastic bronchitis had been made. On previous admissions the chief findings were cyanosis, wheezing and bronchial rales over both lung fields. The heart was not

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enlarged, but the electrocardiogram showed signs of right ventricular strain. Circulation time and venous pressure were normal. The red blood cell count was 5,500,000. Three weeks before his present admission he noted fever which persisted until admission. During this period he suffered from severe cough, marked shortness of breath, severe headaches and pounding sensations in his head.

Physical examination disclosed a well nourished male, propped up in bed, temperature 38.8° C, pulse 120 per minute, blood pressure 120/70, respirations 28 per minute. He appeared acutely ill and was dyspneic at rest. There was marked cyanosis of the face, lips, ears and fingers. The neck veins were markedly congested. The area of cardiac dullness could not be exactly determined because of the marked emphysema. The heart sounds were normal, the second pulmonic sound was accentuated. The chest was barrel shaped with practically no expansion and the lung borders were lower than normal. The breath sounds were distant over both lungs with a prolonged expiratory phase. There were sibilant and sonorous ronchi. Over the lower half of the right lung field, coarse and medium crepitations were heard. The liver edge was three finger-breadths below the costal margin and tender. The spleen was two finger-breadths below the costal margin. The extremities were normal. There were "watchglass" nails.

Laboratory data—Urine analysis, normal, R B C 6,810,000, hemoglobin, 17.5 g per cent, hematocrit, 60, leucocytes, 18,100 with 60 per cent neutrophils, 1 per cent eosinophils, 1 per cent basophils, 30 per cent lymphocytes and 8 per cent monocytes. Sedimentation rate was 3/5 Westergren. Kahn serological test was negative. Blood urea, sugar and protein were normal. A sputum culture revealed *N. catarrhalis* and *staphylococcus citreus*.

X-ray film of the chest on admission showed diffuse cloudiness in the lower part of the right lung, increased markings of the hila and a small amount of fluid in the right costophrenic sulcus. The electrocardiogram showed sinus tachycardia, P pulmonale and signs of right ventricular hypertrophy. Circulation time was 15 sec, antecubital venous pressure 22.5 cm H<sub>2</sub>O.

The presumptive diagnosis was bronchopneumonia, emphysema and spastic bronchitis.

Treatment with penicillin, 600,000 units daily, was instituted and oxygen was administered intermittently. On the third day after admission phlebotomy of 350 cc was performed. On the same day the temperature dropped to normal and his condition started to improve. On June 1st, six days after admission, the venous pressure was 11 cm H<sub>2</sub>O and the liver edge was now palpable one finger-breadth below the costal margin. On June 5th, the x-ray showed clear lung fields. The clinical improvement continued, and on June 15th the venous pressure was 6.5 cm H<sub>2</sub>O. He had lost 3 kg in weight and was discharged in a markedly improved condition.

### *Pulmonary Function Tests*

The results are summarized in Table I. The ventilatory function tests performed seven months before his present admission showed a marked reduction in vital capacity and maximum breathing capacity which were 25 and 17 per cent respectively of the predicted normal values. At the time of his present admission vital capacity and maximum breathing capacity had decreased further to 21 and 13 per cent respectively of the predicted normal values. The expiratory slope of the spirogram was markedly prolonged (Fig 1). The oxygen saturation of the arterial blood was 55.2 per cent and the CO<sub>2</sub> content was 61.32 Vol per cent. Four days later, after the temperature dropped to normal, the oxygen saturation rose to 69.7 per cent and the CO<sub>2</sub> content was 66.67 Vol per cent. After breathing 100 per cent oxygen, the saturation rose to 90 per cent. Two weeks after his admission the oxygen saturation was 85.2 per cent and the CO<sub>2</sub> content had dropped to 57.7 Vol per cent. After exercise the oxygen saturation rose to 86.2 per cent. Marked improvement in ventilatory function was manifested by the increase of vital capacity and maximum breathing capacity, which were now 33 and 19 per cent respectively of the predicted normal values. The expiratory slope of the spirogram was still very pro-

longed (Fig 1) At a control examination five months later, nearly the same values were obtained The oxygen saturation was now 86.5 per cent and rose to 99 per cent after oxygen breathing

### *Effects of ACTH Treatment*

Treatment with adrenocorticotrophic hormone during his previous admission half a year ago, caused marked improvement in the ventilatory function tests The vital capacity and maximum breathing capacity increased by 9 and 5 per cent respectively of the predicted normal values (Table I) The same treatment during his present admission, after recovery from congestive heart failure, caused a decrease in the vital capacity from 33 to 26 per cent and in the maximum breathing capacity from 19 to 15 per cent The oxygen saturation decreased from 85.2 to 83 per cent and after exercise it dropped further to 80 per cent

### *Comment*

This patient was known to have suffered for years from chronic bronchitis and obstructive emphysema Signs of myocardial decompensation had not been seen previously During his present admission, a diagnosis was made of pneumonia accompanied by an exacerbation of chronic bronchitis The acute infection caused a marked deterioration of pulmonary function, manifested by reduction of ventilatory function tests, carbon dioxide retention and anoxia The chief cause of the anoxia was apparently pneumonia associated with a large area of unventilated but well perfused lung parenchyma This probably caused an admixture of unoxygenated venous blood from the pulmonary artery with blood from well ventilated alveoli, a situation analogous to a veno-arterial shunt, as seen in congenital heart disease<sup>9 10 11</sup> The fact that breathing of 100 per cent oxygen increased the oxygen saturation only to 90 per cent speaks in favor of this assumption and makes it improbable that the arterial oxygen unsaturation was due only to faulty distribution or diffusion<sup>12</sup> It should

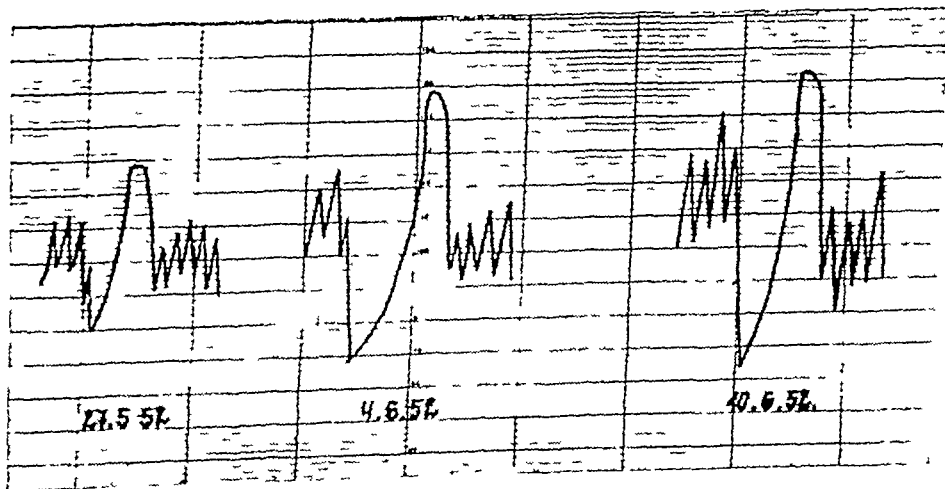


FIGURE 1, Case 1 Spirograms in the course of the disease, showing an increase in the vital capacity without marked change in the contour of the expiratory slope

be pointed out that five months later the oxygen saturation after 100 per cent oxygen breathing rose to 99 per cent

At the time of the pulmonary infection signs of congestive heart failure appeared for the first time. With the recovery from the pulmonary infection, the anoxia gradually diminished and the oxygen saturation rose to the same level as at his control examination and the ventilatory function tests improved markedly. The presence of some oxygen unsaturation even after clinical recovery from the pulmonary infection might be explained by the continuation of pulmonary consolidations and spastic bronchitis. Pulmonary infiltrations have been frequently observed by x-ray studies and confirmed by pathological examinations even after the temperature has dropped to normal, because of the slow resorption of the alveolar exudates<sup>13</sup>. The above observations suggested that in this case pneumonia with an accompanying veno-arterial shunt was the main cause of the pulmonary dysfunction and anoxia.

The different responses to treatment with adrenocorticotrophic hormone in two different stages of the disease was well demonstrated in the lung function tests. On his previous admission, when the presenting disease was bronchial asthma without signs of heart failure, treatment with ACTH caused marked improvement. At his present hospitalization, when the patient was recovering from a bout of congestive heart failure, the same treatment led to a reduction of the ventilatory function tests and an impairment of the respiratory function tests. The cause for this deterioration might be sought in the increased tendency for salt and water retention during this particular phase of the disease, which probably resulted in interstitial edema and pulmonary insufficiency. This notion conforms with the observations of Lucas and Galdston et al, who also found a deterioration of pulmonary function after treatment with ACTH in cases with pulmonary heart disease<sup>14, 15</sup>.

*Case 2* M K, a 65 year old male Jew, was admitted on December 12th 1952, because of shortness of breath and cough. It was not possible to get a detailed history from him or his relatives. He was living in poor economical conditions and had suffered coughing attacks for years.

At the time of admission his temperature was 36.9° C, pulse 104, blood pressure 125/85, respiratory rate 44, weight 70.6 kg. He was dyspneic and orthopneic. There was marked cyanosis of the face, lips, fingers and toes. The fingernails had a "watch-glass" appearance. The neck veins were markedly distended. The chest was barrel shaped and extended poorly bilaterally. The breath sounds were vesicular with prolonged expiration and there were diffuse bronchitic rales. Over the right lung base there was an area of dullness of three fingers breadth with bronchial breath sounds and crepitations. The heart was enlarged in all directions, there were no murmurs, the second pulmonary sound was accentuated. The liver edge was five finger-breadths below the right costal margin and tender. There were ascites and three plus pretibial edema.

An x-ray film of the chest (Fig 2A) showed dilatation of the right and left heart with straightening of the left border and prominence of the right lower border, increased pulmonary hilar markings, especially on the right side, a density in the right lung base and fluid in the right costophrenic sulcus. The electrocardiogram showed P pulmonale and right ventricular hypertrophy.

On admission the red cell count was 4,900,000, hemoglobin 14.0 g per cent, hematocrit, 52, leucocytes, 24,400 with 59 per cent neutrophils, 2 per cent bandforms, 4 per cent eosinophiles, 34 per cent lymphocytes and 1 per cent monocytes. The urine showed 2+ positive albumin, some leucocytes and erythrocytes. The sedimentation rate was  $\frac{1}{2}$  Westergreen. The Kahn serological test was negative. The blood urea was 52 mg per cent, blood sugar 87 mg per cent, NaCl, 525 mg per cent, protein, 5.85 g per cent, albumin, 3.2 g per cent and globulin, 2.65 g per cent. Circulation

time was 22 sec, venous pressure on admission was 22 cm H<sub>2</sub>O. Three days after admission his temperature rose to 38° C and after three days dropped to normal. The presumptive diagnosis was bronchopneumonia, emphysema and spastic bronchitis.

On the first day after admission, because of his serious condition, the patient was given 2 cc of a mercurial diuretic and a phlebotomy of 400 cc was performed. He was placed on a low salt diet, was given 0.9 g aminophyllin daily, oxygen was administered intermittently and penicillin treatment was instituted. On the sixth hospital day digitalization was begun. He received 16 cm digilanide during a period of three days and thereafter 0.1 mg digitoxin daily orally. Eight days after admission his condition started to improve, the cyanosis decreased, urine output increased and the edema began to regress. On December 23rd, the venous pressure was 16 cm H<sub>2</sub>O and the circulation time was 14 sec. During the following two weeks his weight dropped from 67.0 kg to 53.0 kg. All the signs of congestive heart failure disappeared and there was no visible cyanosis. The venous pressure dropped to 5 cm H<sub>2</sub>O. The physical signs over the lungs became normal. A control x-ray film on January 2nd, 1953 (Fig 2B) showed a normal size and configuration of the heart with clear lung fields, increased hilar markings and evidence of emphysema. The electrocardiogram revealed again right ventricular hypertrophy.

### *Pulmonary Function Tests*

The results are summarized in Table II. The first examination was performed four days after his admission. The ventilatory functions tests showed marked reduction. The maximum breathing capacity was 16 per cent and the vital capacity 30 per cent of the predicted normal values. The spirogram exhibited a marked prolongation of the expiratory slope (Fig 3). The oxygen saturation of the arterial blood was 71 per cent at rest and dropped to 63 per cent after exercise. After breathing 100 per cent oxygen the saturation rose to 98 per cent. The carbon dioxide in the blood was 66.3 Vol per cent, indicating marked retention. Five days later the arterial oxygen saturation rose to 82.5 per cent and exercise caused a drop to 70 per cent. Eleven days after the first examination the vital capacity rose to 45 per cent of the predicted value. The oxygen saturation was now 83 per cent and exercise caused a drop to 80 per cent. On January 7 the ventilatory tests showed further improvement. The vital capacity was now 50 per cent and the maximum breathing capacity 30 per cent of the predicted normal.



FIGURE 2A



FIGURE 2B

Figure 2A, Case 2. X-ray film of the chest on admission. See text. Figure 2B, Case 2. X-ray film after recovery. See text.

values. The spirographic tracing showed a normal expiratory slope (Fig 3). The arterial oxygen saturation was now 90 per cent, rising after exercise to 90.5 per cent and the carbon dioxide content was normal.

### *Comment*

This patient was admitted to the hospital in a state of severe cardiac failure and dilatation of the heart. On the basis of clinical and x-ray findings, a diagnosis of spastic bronchitis and pneumonia was established. There was marked reduction of the ventilatory function tests, oxygen unsaturation and carbon dioxide retention. The spirogram showed a marked prolongation of the expiratory slope indicating bronchial obstruction. The oxygen unsaturation was corrected by the administration of 100 per cent oxygen, which justified the assumption that the main cause for the anoxia was faulty distribution or diffusion of air. With the subsidence of the pulmonary infection there was a gradual improvement in the ventilatory function tests and also the expiratory slope became normal, indicating relief from the ventilatory obstruction. The arterial oxygen saturation gradually returned to normal values and the carbon dioxide retention decreased. Accompanying the improvement of the pulmonary functions, the signs of congestive heart failure disappeared, the venous pressure and the circulation time became normal, the urine output increased and there was a marked loss in weight. The x-ray films revealed now a normal configuration of the heart. Table III illustrates the correlation between some pulmonary tests, circulatory measurements and the body weight. The lack of polycythemia in this case might be explained by the poor nutritional state, indicated also by the low blood protein levels. It might be assumed that the chief cause of the acute deterioration in the pulmonary functions in this case was bronchial obstruction, since the anoxia was completely corrected by oxygen breathing and the expiratory slope became normal after recovery from the acute infection.

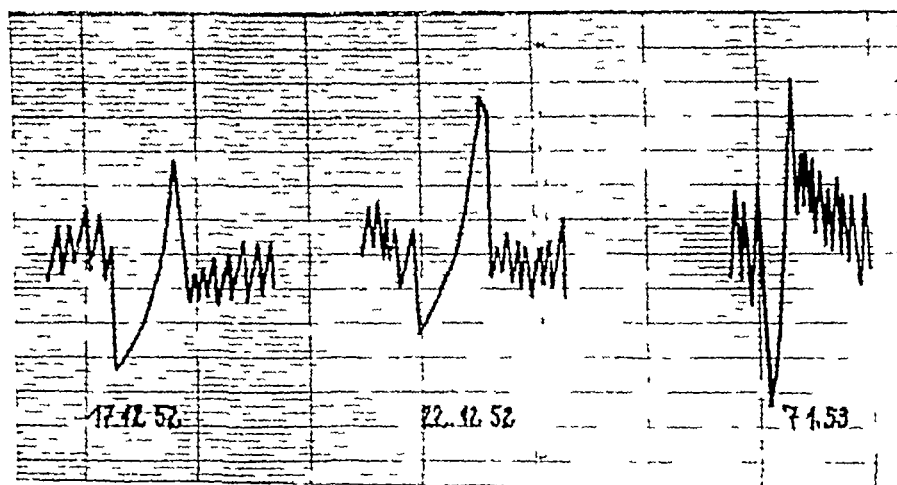


FIGURE 3, Case 2. Spirograms in the course of the disease showing an increase in the vital capacity and a normalization of the expiratory slope.

Discussion

Two patients are presented with signs and symptoms of severe cor pulmonale. In both of them chronic bronchitis and emphysema were present before the appearance of the current disease. Acute pulmonary infection, in one case predominantly pneumonia, in the other predominantly severe obstructive bronchitis, precipitated the appearance of severe congestive heart failure. In these two patients the preexisting chronic lung disease

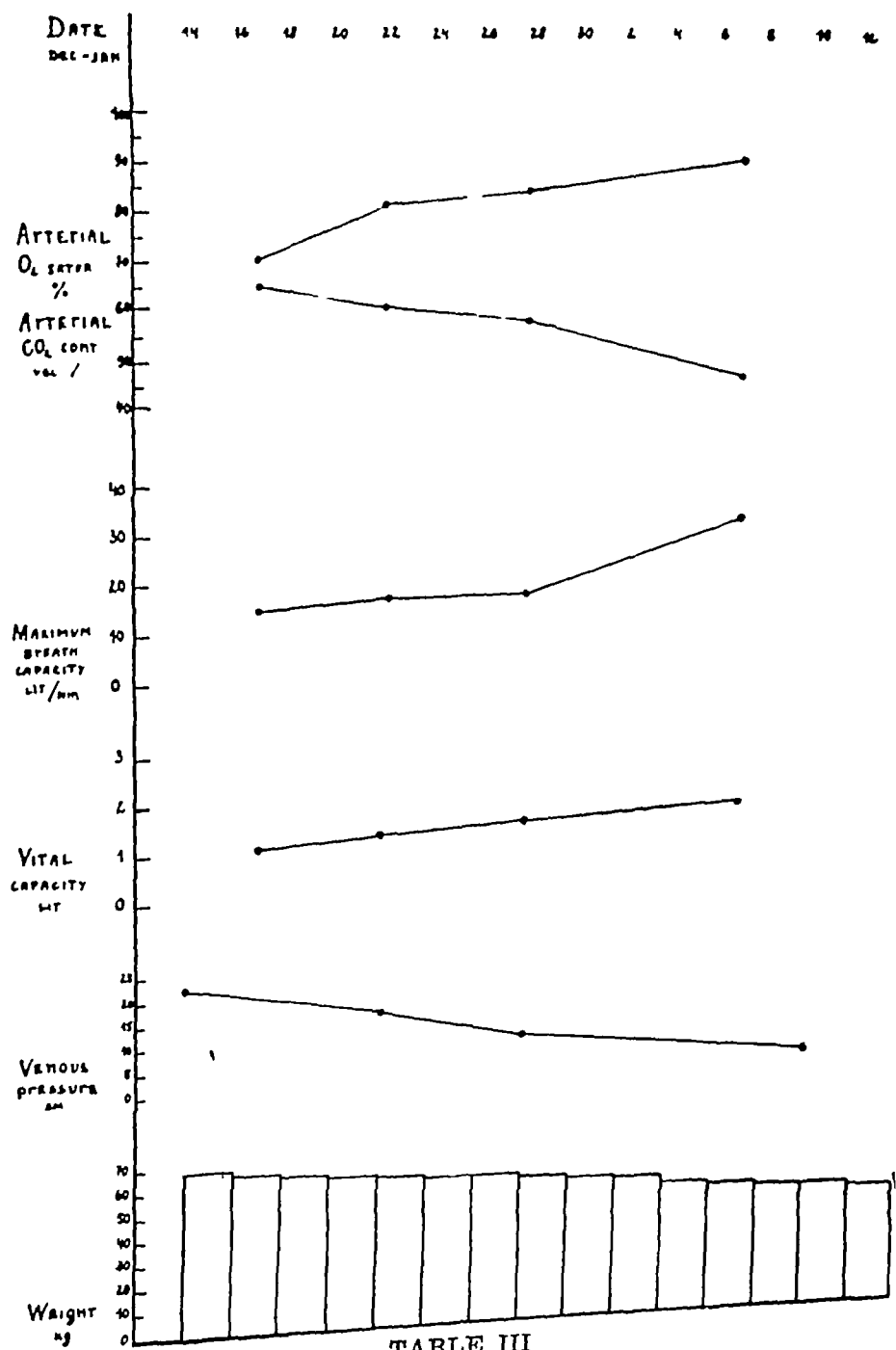


TABLE III

Correlation between circulatory measurements, some pulmonary function tests and body weight

had probably caused a reduction of the pulmonary vascular tree, long before the appearance of heart failure. This reduction resulted in an increased load on the right ventricle and induced right ventricular hypertrophy which was demonstrated in the electrocardiograms taken before and after the present acute illness.

Three factors were probably responsible for the development of acute congestive heart failure in these cases who suffered from chronic emphysema.

I The decrease of the functional pulmonary parenchyma as a result of pneumonia and bronchial obstruction caused further diminution of the already reduced pulmonary vascular tree and thus a greater resistance in the pulmonary circuit. These factors were well demonstrated by the marked reduction of the pulmonary function tests, manifested by the low vital capacity and maximum breathing capacity.

II The fever, induced by the pulmonary infection, caused a rise in the oxygen consumption as a result of increased metabolic requirements. This rise in oxygen consumption is generally accompanied by increased cardiac output, which in turn may lead to an increased pulmonary blood flow and embarrassment of the pulmonary circulation.

III The third factor and probably the most important one was the anoxia. It has been shown that anoxia, apparently by direct action on the pulmonary vessels, augments their vasomotor tone and thereby increases the pulmonary artery pressure.<sup>16, 17</sup> This effect should be more marked in patients in whom there is already a reduction of the pulmonary vascular bed. Other sequelae of anoxia include hypervolemia, increased cardiac output and polycythemia. The first two of these latter increase the volume of blood in the pulmonary circulation and limit further the

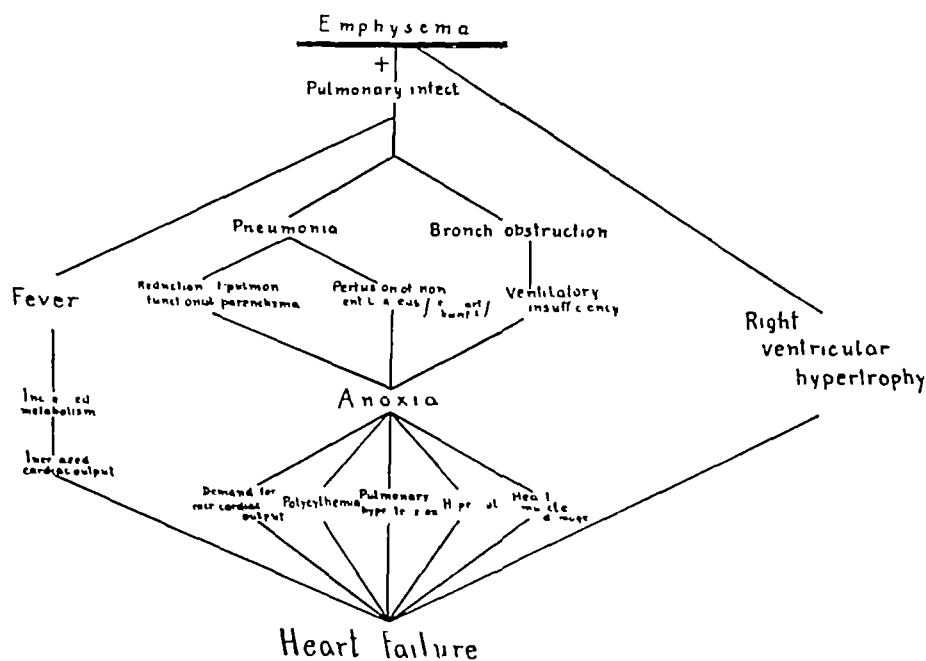


FIGURE 4 Interrelation between the various factors causing heart failure in chronic pulmonary disease complicated by pulmonary infection



capacity of the pulmonary vascular bed Polycythemia,<sup>18, 19</sup> with increased blood viscosity, augments the resistance to flow and raises the pulmonary artery pressure These various mechanisms combine to produce pulmonary hypertension Right ventricular dilatation and cardiac failure result when the hypertrophied right ventricle, whose function is impaired by the direct action of the anoxia on the myocardium, is no longer capable of coping with the overload of the increased pulmonary resistance and the demand for increased cardiac output<sup>20, 21</sup>

The interplay of these various mechanisms in the genesis of heart failure is illustrated in Fig 4 Since there is no intrinsic disease of the heart muscle, as in rheumatic and arteriosclerotic heart disease, the cardiac failure is reversible following the removal of the cause of the acute pulmonary insufficiency. These two patients offered an exceptional opportunity to illustrate the parallelism between the severity of pulmonary insufficiency and the degree of congestive heart failure

### SUMMARY

Two cases of chronic emphysema in which pulmonary infection resulted in acute congestive heart failure have been presented The predominant lesion in one case was pneumonia, and in the second obstructive bronchitis The sequence of events resulting in heart failure are discussed

The technical assistance of Mrs K Galewski and Miss L Beck is acknowledged with gratitude

### RESUMEN

Se presentan dos casos de enfisema crónico en los que la infección pulmonar trajo como consecuencia una insuficiencia congestiva aguda del corazón La lesión predominante fué en un caso, neumonía, y en el otro, bronquitis obstructiva Se discuten series de eventos que condujeron a la insuficiencia cardíaca

### RESUME

Les auteurs rapportent deux cas d'emphysème chronique dans lesquels l'infection pulmonaire eut pour résultat une insuffisance cardiaque congestive aigue La lésion prédominante était dans un cas une pneumonie, et dans le second une bronchite obstructive Les auteurs étudient la succession des circonstances qui entraînent une insuffisance cardiaque

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# Acute, Transient Middle Lobe Disease

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The special significance of atelectasis of the middle lobe was first pointed out in 1946 by Zdansky<sup>1</sup> and Brock,<sup>2</sup> independently. Zdansky described two cases of middle lobe atelectasis in adults caused by compression of the middle lobe bronchus by a calcified lymph node. He noted that in children enlargement of a lymph node often causes compression of a major bronchus leading to atelectasis of the entire lobe without any predilection for any one bronchus and lobe. In adults, on the other hand, atelectasis of an entire lobe will occur more frequently in the middle lobe. In the other lobes, only the smaller bronchi will be compressed leading to segmental atelectasis. This can be explained by the fact that in children all the major bronchi are narrow and easily compressible, while of the major bronchi in adults only the middle lobe bronchus is narrow and is rendered even more easily compressible by virtue of the acute angle it forms with the main bronchus. He, therefore, called the right middle lobe "locus minoris resistentiae der Lunge." Zdansky also noted that besides cases of permanent atelectasis of the middle lobe one not uncommonly encounters a patient presenting an acute febrile illness in whom a chest film will reveal atelectasis of the middle lobe, which however, will reexpand after a few days with subsidence of symptoms. Not uncommonly one may find an enlarged lymph node near the origin of the bronchus. It is of interest to note here that Shaw,<sup>3</sup> in his excellent presentation of a "new clinical entity" caused by mucoid impaction of bronchi, reported 10 cases of segmental atelectasis, bronchiectasis and fibroid pneumonitis caused by plugs of mucus obstructing a bronchus of a second order in patients with asthma or chronic obstructive bronchitis. In one of these cases the middle lobe was involved. Brewer in his discussion of this paper reported a similar case.

Brock in "The Anatomy of the Bronchial Tree" also takes note of the frequency of the middle lobe collapse. He points out that the middle lobe bronchus is particularly vulnerable to the effects of glandular enlargement because it lies in the lymphatic pathway from the right lower lobe and is closely surrounded by glands which drain the lower and middle lobes. He mentions, however, that left upper and lower lobe bronchi are also liable to be compressed by the many glands which surround them at their origin.

The first one to coin the term "Middle Lobe Syndrome" was E. Graham<sup>4</sup> who in 1947 reported 12 cases of nontuberculous adults having compression of the middle lobe bronchus by enlarged lymph nodes. All were characterized clinically by hemoptysis and recurrent episodes of pulmonary infection. Atelectasis, fibrosis and bronchiectasis were the pathologic findings. The enlarged compressing lymph nodes showed changes of a chronic non-specific lymphadenitis. He stressed the necessity of investigating all the lobes in each patient.

Paulson and Shaw<sup>5</sup> reported 32 adult patients, on 29 of whom lobectomy was performed. The pathological findings in the lung were the same as described by Graham. However, they found enlarged lymph nodes in only 15 of these cases. They postulate the possibility that the enlarged nodes may be secondary to the inflammation within the lobe. They noted that many of their patients gave a history of previous pneumonia. Duration of symptoms varied from five months to 20 years.

While in Graham's 12 cases and Paulson's 32 patients the disease was non-tuberculous, tuberculosis was considered as the underlying cause of the pathology in the 16 cases reported by Rubin<sup>6</sup> and in the eight patients of Cohen,<sup>7</sup> all of whom were adults. These workers based their diagnosis on the presence of calcified lymph nodes.

In all these reports as well as in the reports of Doig,<sup>8</sup> Brock,<sup>9</sup> Harper<sup>10</sup> and Fietheim<sup>11</sup> the cases were chronic. In this article the writer reports four cases of acute transient atelectasis of the middle lobe with or without acute pneumonitis all of which cleared up completely within one to four weeks.

### *Report of Cases*

*Case 1* H M, a 52 year old male has had a chronic cough for many years with periodic exacerbations during which time sputum would become "thicker and hard to raise." When seen during one such episode in July 1944 (at the age of 44), the physical examination of his chest showed no abnormal findings. The breath sounds were normal. There was no wheezing and no rales were heard. The temperature was normal. Fluoroscopy of the chest and a posteroanterior film were negative. My diagnosis was chronic bronchitis and possible bronchiectasis. Further work-up was refused. The next time he was seen on May 5, 1952, he stated he got along fairly well with his usual symptoms of cough and occasional exacerbations. Lately he noticed increased expectoration but no other symptom. The physical examination was the same as eight years previously, viz negative. Fluoroscopy in the posteroanterior view was essentially negative, except for suspicious shadowing near the right heart border. View in the lordotic position disclosed the characteristic triangular shadow of atelectasis of the middle lobe. Chest films (Fig 5a and b) corroborated this. He was scheduled for bronchoscopy, but he delayed for one week. He returned May 12, 1952 and at that time fluoroscopy was negative in any positioning. Posteroanterior film taken June 16, 1952 (Fig 5c) was negative. Cough and expectoration diminished gradually to the usual amount with fairly good general health.

*Case 2* G D, a 37 year old male was seen February 20, 1953 because of chills and fever five days previously followed by dry cough. On physical examination a few posttussive rales were heard in the right midaxilla. The temperature was normal. Fluoroscopy, posteroanterior and lateral films (Fig 2a) revealed atelectasis of the middle lobe. He was put on antibiotic treatment. On his return 12 days later there were no rales in his chest and fluoroscopy showed considerable clearing of the shadow in the middle lobe. By March 14, 1953 the atelectasis disappeared completely as shown on the posteroanterior and lateral films (see Fig 2b). He is well and working since then.

*Case 3* T H, a 38 year old female who was hospitalized November 27, 1951 because of fever of 103° F of one week duration, and non-productive cough. Posteroanterior and lateral films on admission (Fig 3a) showed evidence of atelectasis of the right middle lobe and pneumonitis in the middle lobe and possibly in the adjacent portion of the upper lobe. The following day the cough became productive and the temperature dropped to normal. Posteroanterior and lateral films taken four days later showed considerable clearing of the pneumonitis. Bronchoscopy was done December 10, 1951. The right middle lobe bronchus was found to be blocked by a plug of mucus. This was removed by suction. On December 20, 1951, a posteroanterior film (Fig 3b) was negative except for a small area of infiltration in the right mediobase. She was discharged as improved. She failed to return for a re-check examination until March 5, 1952. A film taken on that day was entirely negative.

*Case 4* M P, a 47 year old male was first seen on March 3, 1953. He complained of severe productive cough of one month duration, fatigue and loss of 12 pounds of weight and sticking pains in his right chest. Posteroanterior and lateral films (Fig

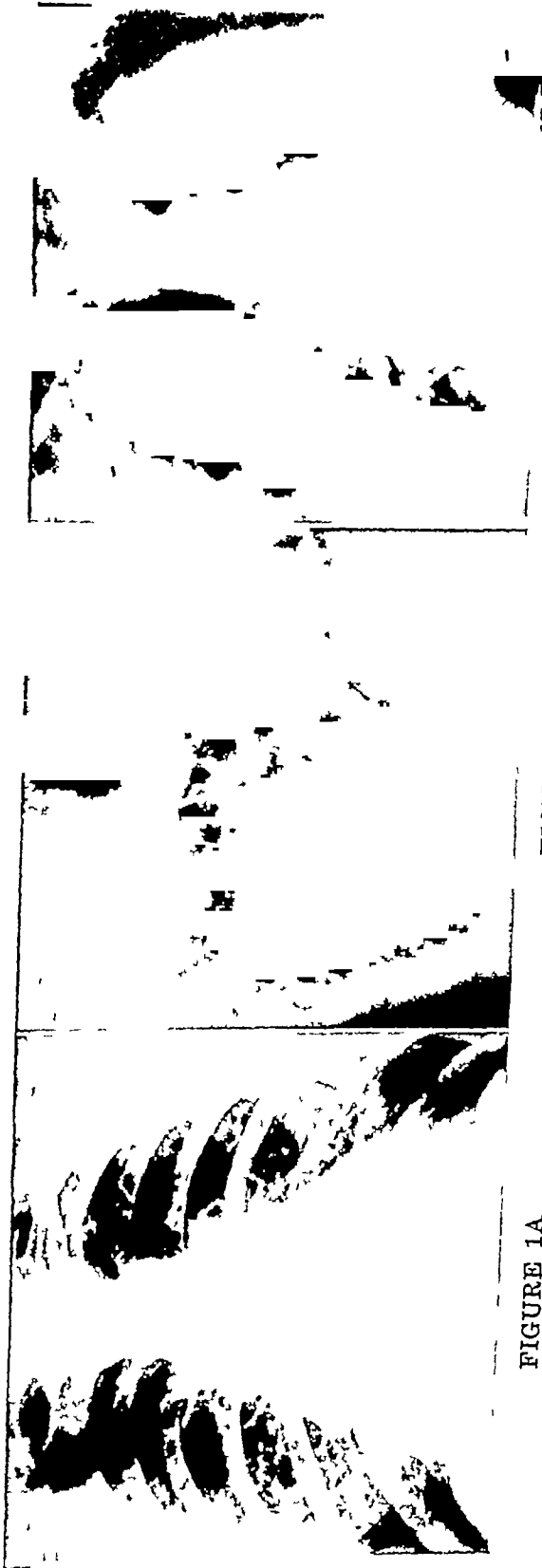


FIGURE 1A

FIGURE 1B

FIGURE 1C

*Figure 1* CASE 1 (a) Posteroanterior film May 5, 1952 shows infiltration near the right cardiac border, which on the lateral film (b) proved to be atelectasis of the middle lobe (c) Posteroanterior film June 16, 1952 shows complete clearing of the infiltration

4a) showed middle lobe atelectasis and pneumonitis. He was referred to a chest surgical clinic for further study. By the time he was given his first appointment in that clinic seven days later, March 10, 1953, a chest film disclosed considerable clearing of the consolidation and infiltration. By March 28, 1953 the chest film (Fig 4b) was entirely negative. He became symptom-free and was discharged from the clinic.

### *Discussion*

Bronchial occlusion leading to atelectasis of the corresponding lobe or segment may occur either by pressure from without, (e g. by an enlarged lymph node or tumor), or by narrowing and obstruction from within, (e g. by edema or fibrous stenosis of the wall or by a plug of mucus occluding the lumen).

A peculiar positioning of a bronchus may make it especially vulnerable to any of these causes of occlusion. Such is the case with the right middle lobe bronchus. It arises from the main stem bronchus at an acute angle and runs in close approximation with the anterior surface of the right lower lobe bronchus for a distance of about 0.75 cm. before curving away from it in an anterior direction. This makes it more vulnerable to compression by the surrounding lymph nodes or to occlusion by a narrowing process within it. Moreover, this positioning may hinder adequate drainage from the inflamed lobe, leading to greater frequency of recurrence and chronicity of pneumonitis in this lobe. This greater frequency of occlusion of the right middle lobe bronchus as compared with the other major bronchi does not occur in children, because in a child all the major bronchi are of a narrow caliber and are easily compressible. Hence, lobar atelectasis in children occurs without any predilection for any one lobe. Such a situation exists also in adults in the case of the smaller secondary or tertiary bronchi, hence, segmental atelectasis in adults occurs with equal frequency in any lobe. It is only in the case of the major bronchi in the adult that a greater frequency of occlusion of the middle lobe bronchus occurs as compared with the other major bronchi. This greater frequency of involvement of the middle lobe justifies the term middle lobe syndrome, even though it may be of varying etiology and pathogenesis. Indeed, if the cases caused by active tuberculous lymphadenitis or bronchitis were to be excluded, one could consider this a disease entity of relatively frequent occurrence.

The name middle lobe syndrome is suggested as an all inclusive term for all cases of middle lobe atelectasis regardless of etiology, and the name middle lobe disease for all cases of atelectasis and pneumonitis which are not caused by active tuberculosis or by neoplasm. While conceivably some cases might have been caused originally by tuberculous lymphadenitis in childhood, the resultant pneumonitis later in life is non-specific and not distinguishable from pneumonitis caused by non-tuberculous lymph nodes or by mucus plugs and poor drainage. Middle lobe disease can thus be defined as characterized by atelectasis and pneumonitis of the middle lobe which may be either transient or chronic with or without accompanying bronchiectasis and caused by poor drainage from the middle lobe due to the peculiar positioning of the middle lobe bronchus.

In every case presenting a history of persistent or recurrent respiratory



FIGURE 2A

FIGURE 2B

*Figure 2 CASE 2 (a) Film taken February 20, 1953 shows atelectasis and pneumonitis of the right middle lobe — (b) March 14, 1953 complete resolution of the pneumonitis and disappearance of the atelectasis*



FIGURE 3A

FIGURE 3B

*Figure 3 CASE 3 (a) Film November 27, 1951 shows pneumonic infiltration in the entire right midlung field — (b) Film December 20, 1951 shows only slight infiltration remaining in the right mediobase (A film taken on March 5, 1952, not shown here, was entirely clear)*

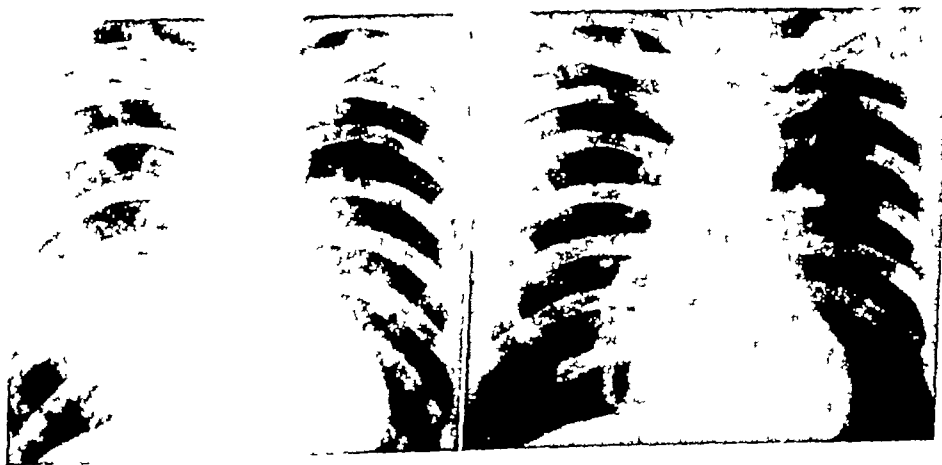


FIGURE 4A

FIGURE 4B

*Figure 4 CASE 4 (a) Film taken March 3, 1953 shows atelectasis and pneumonitis of the middle lobe — (b) Film March 26, 1953, negative*

infection one should, among other diagnoses, entertain the possibility of middle lobe disease. On fluoroscopy of such a patient one should not depend on posteroanterior viewing alone. Quite often the shrunken middle lobe, lying in close proximity with the right heart border, may not be seen in that view—even a posteroanterior roentgenogram may fail to demonstrate it. It is, therefore, imperative also to fluoroscope in the lordotic position and take films in the lateral position.

Middle lobe disease should be differentiated from atelectasis caused by active tuberculous lymphadenitis or bronchitis and from that caused by bronchogenic carcinoma. The latter should be considered first in every case of atelectasis occurring in a middle-aged or elderly individual. However, in middle lobe atelectasis carcinoma is a less likely finding. Brock found that out of 1200 cases of bronchogenic carcinoma, only eight were in the middle lobe. Perhaps this is only a relative infrequency, due to the fact that atelectasis from various other causes is so much more frequent in the middle lobe.

Once the diagnosis of middle lobe disease has been established, one should make a thorough search for involvement in any of the other lobes. Bronchography should be done whenever feasible to rule out bronchiectasis in any other lobe, especially in cases of chronic pneumonitis considered for surgery. Bronchoscopy should be done in every case.

#### SUMMARY

- 1 Four cases of acute transient middle lobe disease have been presented.
- 2 The name middle lobe syndrome is suggested as an all inclusive term for all cases of middle lobe atelectasis regardless of etiology, and the name middle lobe disease for all those cases of atelectasis and pneumonitis which are not caused by active tuberculosis or by neoplasm.
- 3 Attention is being called to the fact that a considerable number of cases of middle lobe atelectasis may be of an acute and reversible nature. Due to the peculiar positioning of the middle lobe bronchus, drainage from an infected middle lobe is poor and mucus plug formation is frequent. As soon as the plug is expectorated or as soon as free drainage is reestablished, the lobe reexpands and a more favorable condition for the clearing of the pneumonitis is created. It is possible that chronic pneumonitis with or without atelectasis of the middle lobe (the latter may be obscured by the enlarged volume of the consolidated lobe) occurs as a result of failure of reestablishing free drainage. Bronchoscopy may be a therapeutic measure in some of these cases, in addition to being a diagnostic procedure.
- 4 Emphasis is placed on the importance of fluoroscopy in the lordotic position, since posteroanterior viewing may fail to demonstrate the shrunken middle lobe. A lateral film is of importance to establish the definite site of pneumonitis and atelectasis.

#### RESUMEN

- 1 Se han presentado cuatro casos de enfermedad aguda, transitoria del lobulo medio.
- 2 Se sugiere el nombre de síndrome del lóbulo medio como término que



incluye todos los casos de atelectasia del lóbulo medio sin tener en cuenta su etiología; y el nombre de enfermedad del lóbulo medio para todos los casos de atelectasia y de neumonitis que noson causados por tuberculosis o neoplasia

3 Se llama la atención sobre el hecho de que un número considerable de casos de atelectasia del lóbulo medio, pueden ser agudos y reversibles. Debido a la peculiar posición del bronquio del lóbulo medio la canalización de ese lóbulo es deficiente y de ahí el taponamiento con masas mucosas. Tan pronto como el tapón es expectorado cuando la canalización se restablece, se reexpande el lóbulo se crean condiciones favorables para la limpieza y curación de la neumonitis. Es posible que la neumonitis crónica con o sin atelectasia del lóbulo medio (siendo este susceptible de ser enmascarado por una área de consolidación más extensa) ocurra como resultado de la falta de restablecimiento de la canalización.

La broncoscopia puede ser un procedimiento terapéutico en algunos de estos casos, además de ser un método de diagnóstico.

4 Se hace énfasis sobre la importancia de la fluoroscopia en la posición de lordosis puesto que el aspecto anteroposterior, puede dejar de mostrar el lóbulo medio retraído.

Una película lateral es de importancia para establecer con precisión la ubicación de la neumonitis y de la atelectasia.

#### RESUME

1 L'auteur rapporte quatre observations d'atteintes du lobe moyen réalisant une évolution aiguë et passagère.

2 Il envisage d'utiliser le terme de "syndrome du lobe moyen" pour toutes les formes comportant une atélectasie de ce lobe, sans tenir compte de son étiologie. Il demande que l'on désigne sous le nom de "maladies du lobe moyen" les atteintes atélectasiques ou pneumoniques, dont l'origine n'est ni la tuberculose évolutive, ni une néoplasie.

3 Il attire l'attention sur le fait qu'un nombre important d'atélectasies du lobe moyen peuvent être dues à un processus aigu et réversible. Etant donné la situation de la bronche lobaire moyenne, le drainage en cas d'infection du lobe moyen se fait mal, et il y a fréquemment constitution d'un bouchon de mucus. Dès que ce bouchon est expectoré, ou dès que le drainage est de nouveau établi, le lobe reprend son expansion et l'ombre pneumonique se trouve dans des conditions qui lui permettent de s'éclaircir. Il est possible que l'absence de rétablissement d'un drainage normal soit la cause de la pneumonie chronique. Celle-ci pouvant ou non s'accompagner d'atélectasie du lobe moyen (ce lobe peut être masqué par l'expansion du reste du poumon). Outre sa valeur diagnostique, la bronchoscopie peut avoir un intérêt thérapeutique dans certains de ces cas.

4 L'auteur insiste sur l'importance de la radioscopie en position lordotique, la position antéro-postérieure ne pouvant dans certains cas mettre en évidence l'atélectasie du lobe moyen. Un cliché de profil est de la plus grande importance pour montrer le siège véritable de la pneumonie ou de l'atélectasie.

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# Chest X-ray Findings and Some Clinical Aspects in Pulmonary Paragonimiasis\*

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Not less than 200 cases have been diagnosed as pulmonary paragonimiasis since 1947 at the medical department of the National Taiwan University Hospital. Of those, definite diagnosis by positive ova from the sputum accompanied by fairly complete laboratory examinations by means of chest x-ray films, blood sedimentation rate, tuberculin test, sputum examination, white blood count with differential and eosinophilia in pleural fluids or in spinal fluids, if necessary, were worked up in 100 cases. Some of these patients were well followed up for as long as three years. Sputa were negative for acid-fast bacilli in all cases by repeated simple smears or cultures.

## I Chest X-ray Findings

Few studies have been published on the x-ray findings of pulmonary paragonimiasis and none is sufficient to justify conclusions. Moreover there is no agreement among these studies. Bercovitz<sup>1</sup> reported that x-ray inspection of the lungs were disappointing and lipiodol installation showed no cavities. In a mass tuberculosis survey in Shinchu district, which is another endemic place of pulmonary paragonimiasis in Taiwan, Kusunoki et al<sup>2</sup> did not find any abnormality on miniature films of 98 persons in whom the parasite ova were discovered in the sputum. On the other hand, Ando and Yamada<sup>3</sup> reported from rice-sized to bean-sized nodular shadows on the x-ray film study of experimental animals. Wang and Hsieh<sup>4</sup> described six cases of well-defined densities or isolated infiltrations which they thought to be characteristic for this condition. Yokogawa et al<sup>5</sup> also have called attention to the fact that they found circumscribed opacities in the majority of their nine cases.

In our series, we observed that the chest x-ray films of 88 out of 100 cases were more or less abnormal which will further be classified as follows:

### 1 Well-defined Nodules

In this category we include moderately or well-defined, considerably hard, but may be homogeneously or irregular dense round or oval patches or nodules. We have seen this kind of nodules in 59 cases. Their sizes range from 0.5 to 4.0 cm in diameter and may appear more than two in number on a single film (in 45 per cent) or combined with ill-defined opacities. The middle lung fields seem to be a slightly more favorite situation than the upper and lower fields (Table 2). These nodules are

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Presented at the 44th annual meeting of the Formosan Medical Association

usually seen in chronic cases and do not disappear completely although they may change their size and density (Case 3)

Nodules are the most frequent manifestation among the abnormal findings in pulmonary paragonimiasis (Table 1). It is difficult to differentiate these nodules from those of tuberculosis on a single x-ray film. But on some occasions one may get a fairly strong impression that tuberculosis is not likely especially when they are multiple and connected with each other or situated in the lower lung field.

### 2 *Ill-defined or Hazy Opacities*

Ill-defined and soft hazy opacities, homogenous or irregular in their densities may be observed. They are usually 2 to 4 cm or more in diameter, variable in shape and may be multiple in number. We observed this kind of shadow in 29 cases. This kind of shadow may appear at any stage of pulmonary paragonimiasis but especially in early newly discovered cases and they are liable to disappear (Case 1) or decrease in size with residual nodules remainings (Case 3) or reappear in other parts of the lungs by follow-up studies. These shadows are due to the perifocal unspecific inflammation or allergic reaction and are extremely difficult to differentiate from tuberculous infiltration as well as nonspecific bronchopneumonia by single x-ray film inspection. With clinical symptoms we might be able to predict the correct diagnosis even before the discovery of the parasite ova in some of these cases when the x-ray shadows resemble those of bronchopneumonia.

### 3 *Pleurisy*

Pleurisy with or without effusion was observed in 30 cases. Of these, 14 were on the right side, nine on the left and seven on both sides. It is most frequently seen in the early stage when the larva likely penetrate the diaphragm into the pleural spaces and consequently the ova still can not be found in the sputum. Pleurisy may also occur if the "bulow" is situated too near the visceral pleura or the parasites actually lodge in the pleural spaces. Differentiation from tuberculous pleurisy by x-ray film can not be made. However one's suspicion is aroused when it is bilateral and/or accompanied by hazy opacities in the lower lung field, which are uncommon in cases of tuberculous pleurisy.

### 4 *Spontaneous Pneumothorax*

We saw four cases with this condition. All were on the left side. Pleurisy with effusion and soft cloudy opacities in the lung parenchym were

TABLE I ABNORMAL CHEST X-RAY FINDINGS IN 100 CASES  
OF PULMONARY PARAGONIMIASIS

Abnormal Findings	No. of Cases
Well-defined Nodules	59
Ill-defined Opacities	29
Pleurisy	30
Increases Lung Markings	34
Spontaneous Pneumothorax	4
Ring Shadows	2
Calcification	6

combined in all instances. These conditions disappeared in a short time (Case 4). Penetration of visceral pleura by the larva when they gain access into the lung is the most probable etiology.

In addition to the above mentioned, increased lung markings and calcified lesions were seen in 34 and six cases respectively. They were not pathognostic though. Ring shadows indicative of suspected cavitation were only seen in two cases. No case with definite cavitation has been seen.

TABLE II LOCALIZATION OF ABNORMAL DENSITIES  
IN THE LUNG PARENCHYM

Localization	Upper	Middle	Right Lower	Upper	Left Middle	Lower
Nodules	14	26	21	17	17	11
Ill-defined Opa	2	11	6	5	8	4
Calcifications	0	1	2	0	1	2
Total	16	38	29	22	26	17

## II Some Other Clinical Aspects

### 1. Blood Sedimentation Rate

Few references are available concerning this subject. One hour rate in 91 cases of our series at the first visit will be shown in Table 3.

TABLE III BLOOD SEDIMENTATION RATE

BSR	Number of Cases	Mean Value
6—10	27	
11—20	25	
21—50	25	26.0
51—	14	
Total	91	

Blood sedimentation rate was variable and no definite correlation could be found with the type of x-ray shadow, severity of clinical symptoms and treatment. Because of its rather wide range, it is not too valuable in differential diagnosis.

### 2. White Blood Count

In 4 of our cases, there was leucocytosis of more than 10,000 in 26 cases (58 per cent) with the mean value of 12,000. Leucocytosis is apt to subside following treatment but no relationship could be found between leucocytosis and the extent of the x-ray findings or the clinical symptoms at the first consultation. The differential count was within normal limits except the eosinophils which was often markedly increased.

### 3. Eosinophilia

It is generally believed that there is slight eosinophilia in the peripheral blood, but Bercovitz<sup>1</sup> reported the value of one per cent eosinophil from his 20 cases. We obtained an average of 13.6 per cent in 45 cases.

Eosinophils constituted more than 50 per cent of the white cells in

pleural fluid in 8 of our 10 cases who had such blood studies. This finding might be the only way to differentiate from tuberculous pleurisy with effusion in many instances at the time when the diagnosis is still obscure due to the negative result of parasite ova in the sputum.

More than 60 per cent eosinophilia with increase of cell count in the spinal fluid were obtained in two cases of cerebral manifestation. This finding is suggestive of cerebral manifestation of this malady and may be the key point to differentiate from other cerebral conditions.

#### 4 *Subcutaneous creeping tumors*

In nine of 100 cases subcutaneous tumors were found. These were from green-pea to thumbtip in size and fairly firm in consistency. The subcutaneous connective tissue of the abdominal or the chest wall were the most frequent situations. Characteristic is that they may creep from one place to another and may disappear or reappear. The tumor may be single or multiple in number.

*Case 1* S T C, a 43 year old male, visited our out patient department on June 19, 1948 with the complaints of cough, and chest pain for about one month and bloody sputum for two days. No fever elevation was noticed. He had a history of eating undercooked crabs two months prior. Physical examination showed the signs of bilateral pleural effusion which was proved by aspiration. This was a serous exudate but negative for

FIGURE  
1A

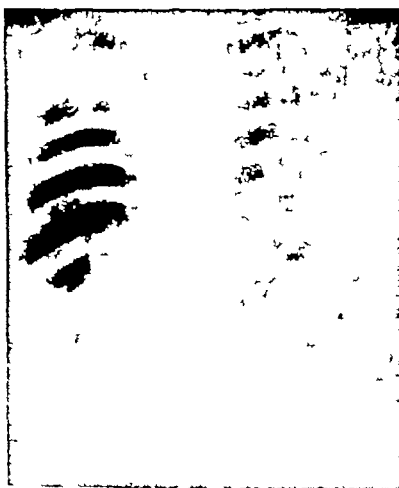


FIGURE  
1B

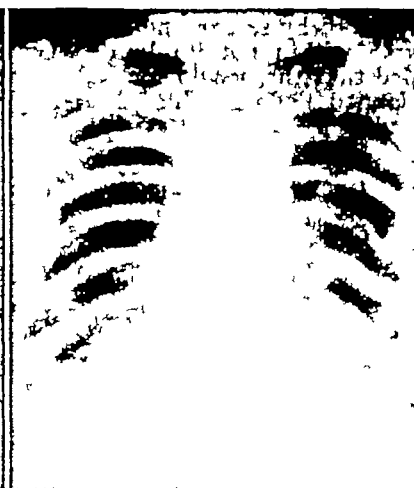


FIGURE  
2A

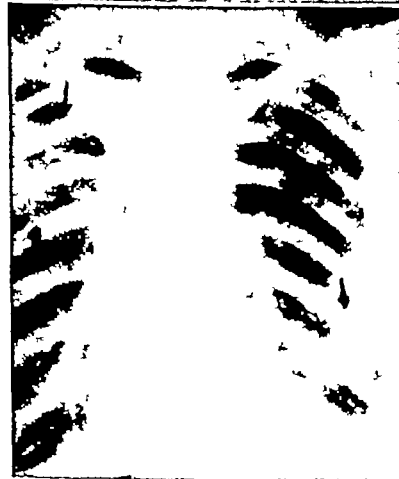


FIGURE  
2B



acid-fast bacilli both by smear and culture. Worthwhile is that eosinophilic leucocytes constitute more than 80 per cent of the cell elements of the effusion. There were 10,100 white blood cells with differential of 16 per cent eosinophils. Blood sedimentation rate was 52 (one hour). Chest x-ray film showed evidence of bilateral pleural effusion with an ill-defined density in the left middle lung field (Fig 1A). Repeated sputum examination for acid-fast bacilli and ova of *paragonimus westermani* had been negative until July 27, when the latter were found in the bloody sputum. Chest x-ray film on August 29 revealed clearing of the pleural effusion bilaterally and condensation of the previous cloudy opacity in the left middle lung field (Fig 1B).

*Case 2* C S C, a 26-year-old male, was admitted in August 1948, complaining of severe cough and bloody sputum for two weeks. He had taken raw crabs in several occasions since 1946. In August 1947 he suffered from chest pain with bloody sputum, thereafter he had recurrent hemoptysis and had been treated as pulmonary tuberculosis. Once, he noticed a finger tip sized tumor in the abdominal wall but not much attention was paid because it disappeared in a few days. Physical examination on admission revealed no abnormal physical sign in the chest or the abdomen. The tuberculin test was positive, the blood sedimentation rate was 43 (1 hour). No fever was noted. There was no abnormal finding in his blood count except 8 per cent eosinophilia. A chest x-ray film taken on August 7 (Fig 2A) revealed an ill-defined opacity, irregular in its homogeneity, throughout the right upper lung field, resembling that of tuberculous infiltration. Well defined nodules also were evident in the left lower lung field. Ova of distoma were found from the sputum but acid-fast bacilli were not demonstrated by 70 smears and 20 cultures. Following the combined therapy of emetine and aktisol, his symptoms were greatly improved although the ova did not disappear completely. A chest x-ray film on September 24 showed almost complete clearing of the abnormal density in the right upper lobe (Fig 2B). He was discharged on December 11.

*Case 3* K S C, a medical student, aged 27, was found to have an ill-defined cloudy opacity in the right middle lung field mesially in December 1949 (Fig 3A). In the summer of that year, he recalled eating undercooked crabs followed by chocolate-colored sputum in which the ova of *paragonimus westermani* were found by himself. Sputa were negative both by smear and culture. White blood count and red blood sedimentation rate were within normal limits. On January 12, 1950 a follow-up x-ray film study revealed that the previous cloudy density had decreased in size and appeared to be a well defined nodule (Fig 3b). He is now a resident of our hospital and a follow-up study in December 1951 showed further minimization of the nodule.

*Case 4* C W S, a male, aged 34, visited our outpatient department on January 21, 1948 with the complaints of chest pain and intense cough. A chest x-ray film taken nine days prior was normal. In view of reduced resonance with diminished breath sound over the left lower chest, another film was ordered on January 30, which showed left spontaneous pneumothorax with pleural effusion and a soft density in the left midlung field (Fig 4A). The fluid was yellowish clear, positive for Rivalta test and negative for acid-fast bacilli by culture. Left pulmonary tuberculosis with spontaneous seropneumothorax had been the diagnosis until white blood count was done a few days later with the result of 14,900 leucocytes and 16 per cent eosinophilia. The

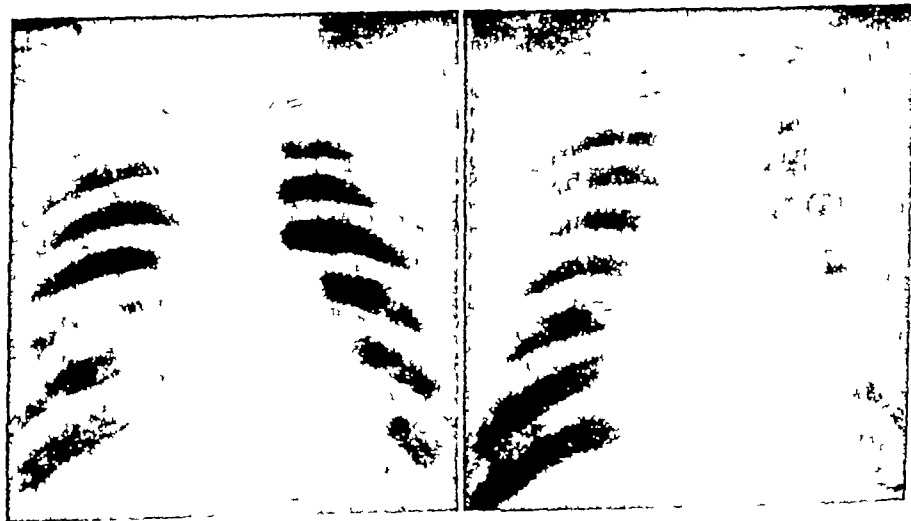


FIGURE 3A

FIGURE 3B

follow-up roentgenological examination on February 16 revealed complete clearing of the seropneumothorax as well as the parenchymal infiltration (Fig 4B). Thereafter he developed right sided pleurisy with effusion (eosinophilia in it) in March and finally was admitted to the medical ward on May 1, for a complete work up of his disease. During his hospitalization, eosinophilia in peripheral blood ranged from 28 to 55 per cent. Acid-fast bacilli were not demonstrated by 50 smears and 15 cultures. A diagnosis of pulmonary paragonimiasis had only been suspected until the discovery of the parasite ova in bloody sputum on September 21.

### SUMMARY AND CONCLUSION

1 Chest x-ray films and some other clinical figures have been studied in 100 cases of proved pulmonary paragonimiasis.

2 Contrary to the previous general belief, x-ray findings of pulmonary paragonimiasis may reveal one or several kinds of abnormalities, namely well-defined nodules, ill-defined transient opacities, pleurisy, spontaneous pneumothorax and ring shadows, provided they are well followed up from the onset of disease.

3 It is difficult to differentiate these abnormalities from those of tuberculosis or bronchopneumonia by x-ray films alone with some exceptional cases in which the impression from the findings as a whole is definitely unlike that of tuberculosis.

4 The incidence of pleurisy with or without effusion is high and it is often the first manifestation. High percentage of eosinophils in the pleural effusion has its diagnostic value to differentiate from tuberculous pleurisy.

5 Slight leucocytosis with differential count of considerable eosinophilia in peripheral blood are rather common.

6 The mean value of blood sedimentation rate in this disease is slightly increased. It has a such a wide range it is not valuable in diagnosis.

7 Eosinophilia in the cerebrospinal fluid may be the key point to differentiate the cerebral complication of this disease from other cerebral conditions.

8 Subcutaneous creeping tumors, if present, are strongly suggestive of this disease in Taiwan.



FIGURE 4A

FIGURE 4B



## RESUMEN

1 Se han estudiado las películas roentgenograficas y otros aspectos clínicos en 100 casos de paragonimiasis demostrada en el pulmón

2 Contrariamente a la ciencia general, los hallazgos a los rayos X en la paragonimiasis pulmonar, pueden revelar varias clases de anomalías, como son nódulos bien definidos, opacidades transitorias mal definidas, pleuresía, neumotórax espontáneos e imágenes anulares, siempre que se busquen desde el principio de la enfermedad

3 Es difícil diferenciar estas anomalías de las de la bronconeumonía o de la tuberculosis sólo por los rayos X, salvo algunos casos en los que la impresión de los hallazgos, es definitivamente disimilar de la tuberculosis

4 La frecuencia de la pleuresia con o sin derrame, esalta y a menudo es la primera manifestación. Un elevado porcentaje de eosinófilos en el líquido pleural, tiene valor diagnóstico para diferenciar de la pleuresia tuberculosa

5 Es común encontrar ligera leucocitosis con una cuenta diferencial mostrando considerable eosinofilia en la sangre periférica

6 La sedimentación globular está ligeramente aumentada

7 La eosinofilia en el líquido cerebroespinal, puede dar la clave para diferenciar la complicación cerebral de esta enfermedad, de otras afecciones cerebrales

8. Los tumores subcutáneos movedizos, cuando se encuentran, son fuertemente sugestivos de esta enfermedad en Taiwan

## RESUME

1 Les auteurs ont étudié les radiographies pulmonaires et quelques caractères cliniques concernant cent cas de distomatose pulmonaire avérée

2 A l'opposé de l'opinion généralement admise jusqu'à présent, les constatations radiologiques dans la distomatose pulmonaire peuvent mettre en évidence un ou plusieurs caractères anormaux, nodules bien délimités, infiltrats labiles, pleurésie, pneumothorax spontané, et ombres annulaires et altérations apparaissent à condition que la maladie soit suivie depuis son extrême début

3 Dans l'ensemble, on ne peut que difficilement différencier ces aspects radiologiques de ceux qui appartiennent habituellement à une tuberculose ou aux pneumopathies aiguës. Ce n'est que dans quelques cas exceptionnels que l'aspect apparait nettement différent de celui de la tuberculose

4 Une réaction pleurale avec ou sans épanchement est fréquente et réalise souvent la première manifestation de la maladie. L'importance de l'éosinophilie du liquide pleural a une grande valeur diagnostique et permet de le différencier de celui de la pleurésie tuberculeuse

5 Dans le sang périphérique, l'existence d'une leucocytose peu élevée avec une éosinophilie considérable est assez commune

6 La vitesse de sédimentation sanguine est, dans cette affection, légère-

ment augmentée. Toutefois, cette augmentation n'atteint pas de proportions suffisantes pour prendre une valeur au point de vue du diagnostic.

7 L'existence d'éosinophilie dans le liquide céphalo-rachidien peut permettre de différencier les complications cérébrales d'autres affections touchant l'encéphale.

8 L'existence de tumeurs sous-cutanées mobiles, si on peut les constater, est tout à fait suggestive de cette affection.

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# Teaching Chest Disease\*

## The Chest X-ray Survey as a Teaching Instrument

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Chest x-ray surveys have proved themselves of considerable value in discovering chest disease. They also contain great teaching possibilities which have received scant attention. In one city the survey was used to demonstrate three significant teaching aspects.

In this survey all individuals who had abnormalities discovered on photo-fluorograms and confirmed with standard roentgenograms were asked to report to a diagnostic clinic. Medical students acted as physicians in this clinic. Here a short history was taken by them for the control records, and sputum and skin test procedures initiated. The patients were shown their roentgenograms which were explained to them by the medical students under the guidance of a senior consultant. This interview served to impress upon the patient the importance of seeing his or her private physician, and following through to thorough understanding and treatment, if indicated, of the roentgen findings. These interviews also introduced the medical students to more new chest pathology, and allowed them to examine more patients with a variety of pulmonary disease in a shorter period of time, than is possible in any other way. They could not help but be stimulated to realize the significance of chest diseases.

A second teaching demonstration by the survey was the revelation to the students and practicing physicians of the amount of thoracic pathology that can be overlooked without roentgen examination. Many of the patients in whom disease was discovered had recently had a "complete examination," but without roentgenologic study of their chests and had been assured they were in good health. The findings of the survey taught an embarrassing lesson to many physicians and students who had been unaware of the great value of routine chest roentgenograms. Unfortunately, this lesson is still to be revealed to many more physicians.

The third educational value of this survey was the accumulation of teaching material for later demonstration of the value of routine chest roentgen examination. We were able to assemble a series of over 90 survey cases, each representing different thoracic abnormalities. This included many of the "normal" variations of chest structure, agenesis of the lung, various effusions, histoplasmosis, coccidioidomycosis, forms of pulmonary tuberculosis and its treatment, silicosis, varieties of cystic disease, "coin" lesions of different etiologies, numerous tumors, malignant and benign, esophageal diseases, sarcoidosis, diaphragmatic abnormalities,

\*The first in a new series of articles prepared under the sponsorship of the Council on Undergraduate Education of the American College of Chest Physicians

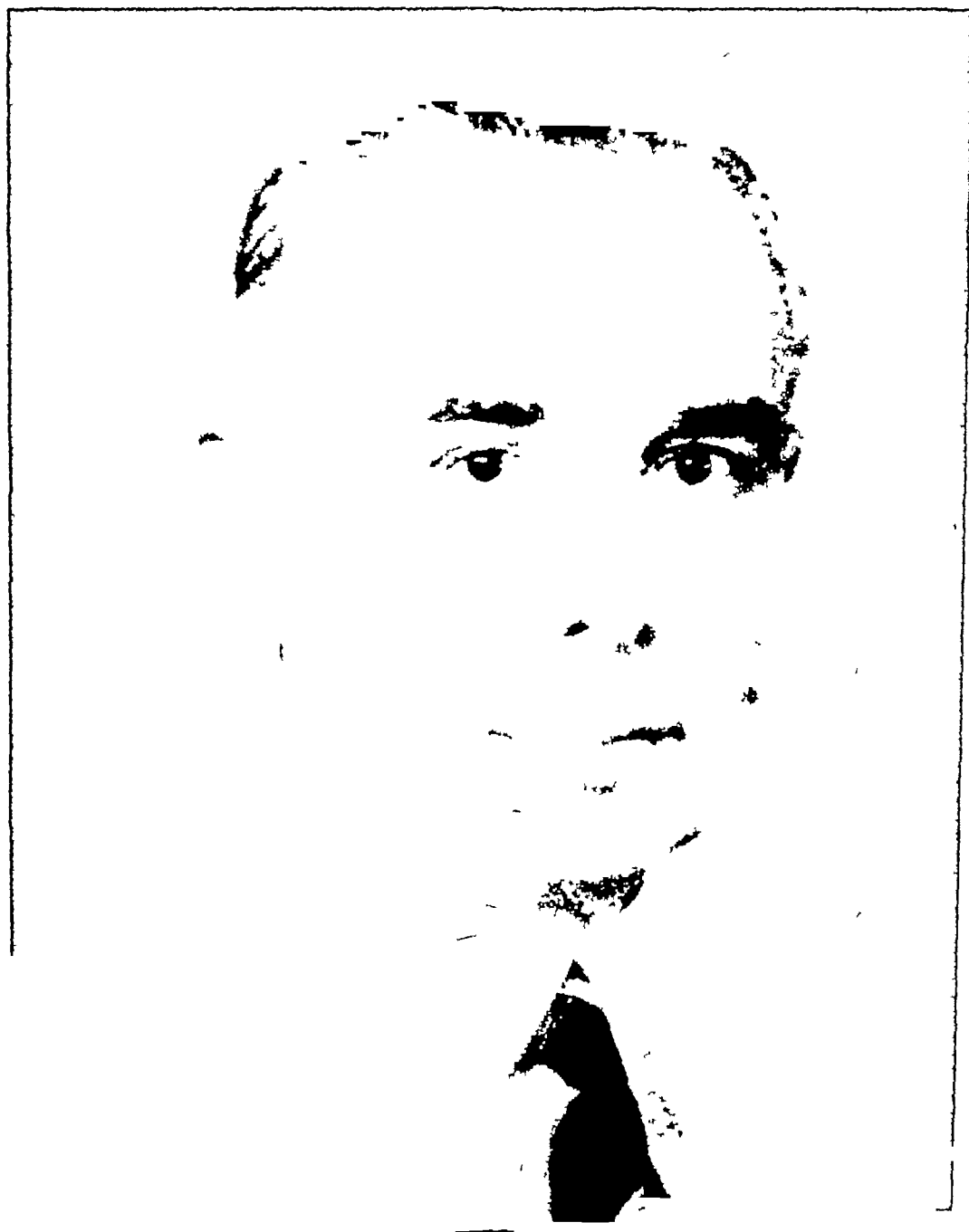
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lib tumors, aneurysms, and a variety of cardiac changes including septal defects, situs inversus, vascular rings, coarctation and the many variations of rheumatic and hypertensive heart disease. In fact, the variety was complete enough to organize the films in such fashion that there was a case to represent nearly all the entities listed in Rubin's *Diseases of the Chest*. It has been presented in that order and entitled "Everything in the Book."

The demonstration of these cases has been especially impressive when one realizes that these were all individuals walking on the streets of an average-sized American city. A similar series can easily be assembled by any routine x-ray unit or center. Presentation of these cases on slides has been enthusiastically received and has initiated plans for routine admission roentgenograms in several institutions.

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RECIPIENT OF COLLEGE MEDAL



Raul F Vaccarezza, M D , F C C P  
Buenos Aires, Argentina

# Presentation of the College Medal to Dr. Raul F. Vaccarezza\*

Mr Chairman, Your Excellencies, Distinguished Officials of the College, Ladies and Gentlemen

As Chairman of the Council on International Affairs of the American College of Chest Physicians, it gives me great pleasure to expedite the awarding of the Medal for outstanding scientific achievement in the specialty of diseases of the chest

This Medal is offered by the College, an international organization, in recognition of exceptional, genuinely original, important work in this field, every two years at the time of the International Chest Congress. We feel gratified to report to this distinguished gathering that after due circumspection and deliberation, selection of a man has been made for this honor

His talent and ability, we are sure, amply deserve this decision. He has been a teacher and educator of medical students for many years. His name as a clinician is well known far beyond the confines of his own community and far beyond the boundaries of his country

Though both of these accomplishments are laudable and admirable, this reward is extended to him because of his renowned research work. Through ingenious foresight, he explored the secrets of the functional capacity of the lung. His endeavors in this direction began many years ago. He approached the problem with the inquisitiveness of a pioneer and the objective perspective of a true scientist. He covered hitherto unexplored territory with the intuition of an artist, with the courage of a good soldier and with the meticulous precision of famous artisans. Through his extensive, indefatigable, investigative studies, new means and methods for measuring pulmonary function have crystallized

The crudeness and uncertainty of earlier empirical methods have been replaced by his scientific endeavors by exactness and precision. His contributions in this respect represent immeasurably valuable tools for everyday use in thoracic surgery, diagnosis and medical management of chest diseases as well as in forensic medicine

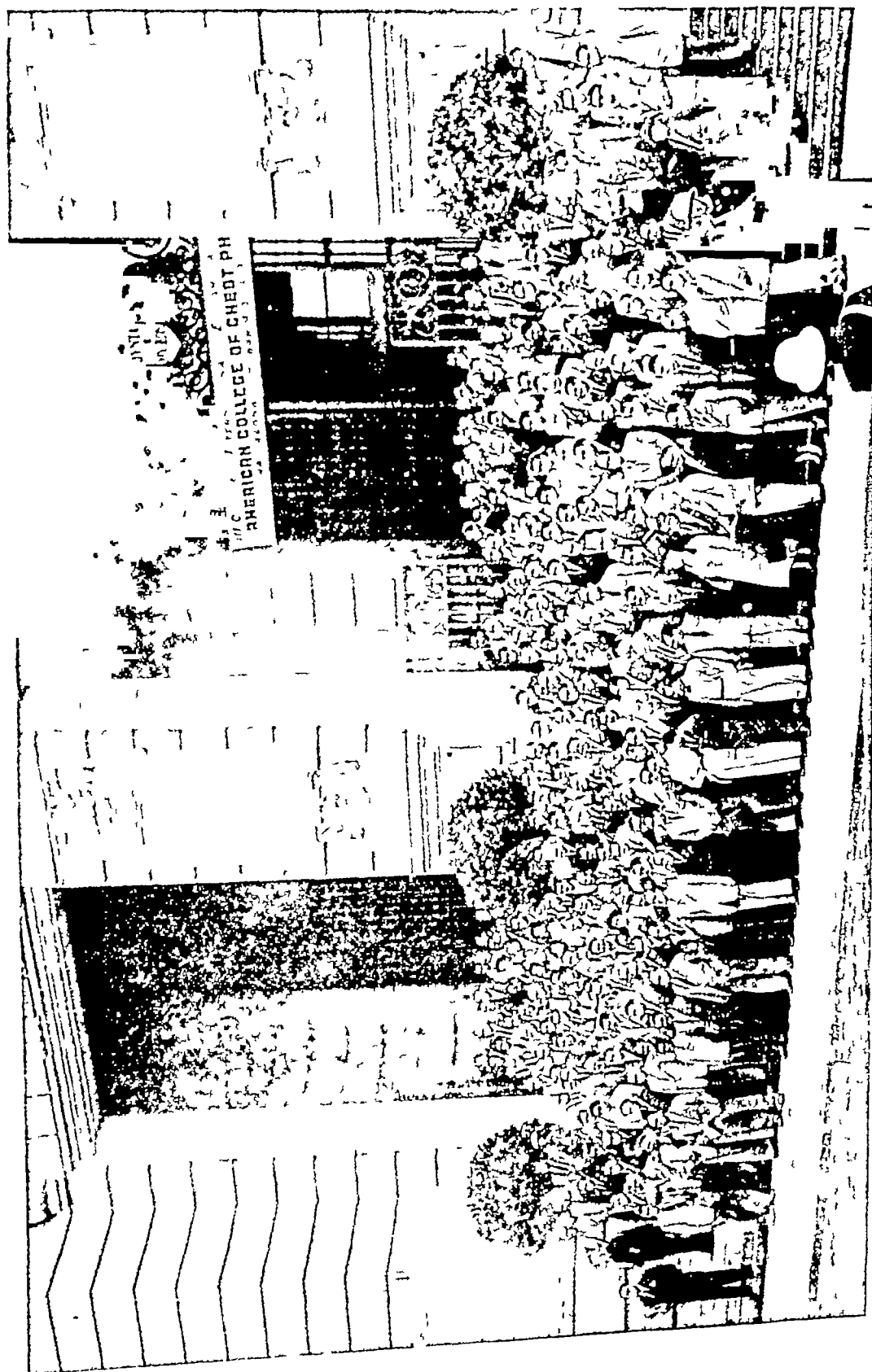
His profound knowledge, his analytical insight and mature prudence have brought him to the forefront of medical activities. Consequently, his affiliations included editorship of medical journals, governorship in the American College of Chest Physicians, presidency of his national chapter and a great many other distinctions. He is a prolific medical writer and the author of more than 250 scientific papers. At the present time he is Professor of Pathology and Clinical Tuberculosis at the Medical School of the University of Buenos Aires, Argentina. Also, he is Director of the Institute of Phthisiology at the same University

Ladies and gentlemen, awarding this Medal is symbolic of the respect and admiration of the membership of this great international organization, the American College of Chest Physicians. To me personally, it is a distinct privilege indeed, to give you the Medal of the American College of Chest Physicians, Professor Raul F. Vaccarezza

ANDREW L. BANYAI, M.D., F.C.C.P.  
Milwaukee, Wisconsin

\*Presented at the Inaugural Ceremony, Third International Congress on Diseases of the Chest, Barcelona, Spain, October 4, 1954

THIRD INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST  
Barcelona, Spain, October 1-8, 1951



Some of the delegates of the Congress photographed at the entrance to the National Palace of Montjuich, Barcelona, where the sessions of the Congress were held

## Third International Congress on Diseases of the Chest

More than two thousand delegates and their wives, representing fifty-nine countries throughout the world, attended the Third International Congress on Diseases of the Chest held in Barcelona, Spain, October 4-8, 1954. The Congress was sponsored by the Council on International Affairs of the American College of Chest Physicians and presented under the patronage of the Spanish Government. Its Honorary Presidency was graciously accepted by the Honorable Generalissimo Francisco Franco, Chief of State of the Spanish Government. The officers of the Congress were Dr. Luis Rosal, Barcelona, Spain, President, Dr. Cristobal Martinez Bordiu, the Marquis de Villaveide, Madrid, Spain, Vice President, Dr. Antonio Calalps, Barcelona, Spain, Secretary General, and Dr. Francisco Coll Colome, Barcelona, Spain, Treasurer. Other officials of the Spanish Government who served in an honorary capacity for the Congress were the following: Hon. Blas Perez Gonzalez, Minister of State, Hon. Joaquin Ruiz Gimenez, Minister of Education, Hon. Alberto Martin Añajo, Minister of the Exterior; and Hon. Gabriel Arias Salgado y de Cubas, Minister of Information and Tourism. The Directors of all Government Services of Spain, the medical schools and medical associations, as well as the ambassadors and consuls represented in Spain, also served as Honorary Members of the Congress.

The solemn Inaugural Ceremony and the scientific meetings were held at the magnificent National Palace of Montjuich. This splendid structure, built in 1929 for an international exposition, stands in a beautiful park on one of the mountains which surround Barcelona. It affords a superb, panoramic view of the city. On the opening night its richly illuminated facade, its flower-decorated and flag-bedecked halls gleamed with the radiance of a crystal castle of fairy tales.

The ceremonies of the inaugural session took place in the immense general assembly hall. Representatives of the Government of Spain, dignitaries of the Provincial Government and the Municipality of Barcelona, Ministry of Health and other prominent functionaries of governmental agencies and the Royal Academy of Medicine and Deans of Medical Schools added emphasis to the importance of the occasion. A large contingent of the Board of Regents and Board of Governors of the College was present.

Nothing could have been more expressive of the unity of purpose of all those present than the melodious chords of the national anthems of the various countries. The resounding tones of the huge organ signaled the opening of the Congress. The high-lights of the evening began with the introductory oration delivered by Dr. Rosal, President of the Congress. Following this, President Eisenhower's message to the Congress was read by Dr. Alvis E. Greer, Houston, Texas, Immediate Past President of the College. Fellowship certificates were given to a large number of chest specialists from Argentina, Australia, Austria, Belgium, Brazil, Colombia, Cuba, Finland, France, Germany, Great Britain, Greece, India, Israel, Italy, Japan, Lebanon, The Netherlands, Philippine Islands, Portugal, Spain, Sweden, Switzerland, Turkey, Venezuela and the Union of South Africa.

The International Award of the College Medal for outstanding scientific contribution was given to Dr. Raul F. Vaccarezza, Professor of Pathology and Clinical Tuberculosis at the Medical School of Buenos Aires, Argentina.

The next speaker was Dr. William A. Hudson, Detroit, Michigan, President of the College, who on behalf of the officers and membership, conveyed his thanks and grateful appreciation. A most hearty welcome was extended to the Congress by the Mayor of Barcelona, Senor Simarro. Finally, the Civil Governor, Senor Felipe Acedo Colunga, representing the Spanish Government as well as on his own behalf, greeted the participants and declared the Congress open. Following the formal Inaugural Ceremony, a reception was given in the beautiful marble rotunda on the second floor of the National Palace.



## SPANISH DIGNITARIES AT INAUGURAL CEREMONY



Inaugural Ceremony, Third International Congress on Diseases of the Chest. The Civil Governor of the Province, the Mayor of Barcelona, and other Spanish Dignitaries were seated at the above table of honor

## COLLEGE OFFICIALS AT INAUGURAL CEREMONY



Left to right Dr Joachim Hein, Germany, Dr Gumeisindo Sayago, Argentina, Dr Donato Alarcon, Mexico, Dr James H Stygall, U S A , Dr Etienne Bernard, France, Dr Alvis E Greer, U S A



Left to right Dr Antonio Crespo Alvarez, Spain, Dr Eugenio Morelli, Italy, Dr Antonio Caralps, Spain, Dr William A Hudson, U S A , Dr Luis Rosal, Spain, Dr Raul F Vaccarezza, Argentina



Left to right Dr Raul F Vaccarezza, Argentina, Dr Andrew L Banyai, U S A , Dr Manoel de Abreu, Brazil, Dr Lopo de Carvalho, Portugal, Dr Donald R McKay, U S A , Dr P E A Nylander, Finland, Dr Burgess L Gordon, U S A , Mr Murray Kornfeld, U S A

## PRESIDENT HUDSON ADDRESSES CONGRESS



Dr. William A. Hudson, Detroit, Michigan, President of the American College of Chest Physicians, addressing the Inaugural Ceremony. At extreme right, Dr. Luis Rosal, President of the Congress.

PRESIDENT EISENHOWER'S MESSAGE READ



Dr. Alvis E. Greer, Houston, Texas, Immediate Past President of the College, reading the message received from Dwight D. Eisenhower at the Inaugural Ceremony

## DR. VACCAREZZA RECEIVES COLLEGE MEDAL



Dr Raul F Vaccarezza, Buenos Aires, Argentina, being introduced by Dr Andrew L Banyai, Milwaukee, Wisconsin, Chairman of the Council on International Affairs, when he was awarded the College Medal at the Inaugural Ceremony. At extreme left, Dr Luis Rosal, Barcelona, President of the Congress. At extreme right, Dr Manoel de Abreu, Rio de Janeiro, Brazil, President of the Second International Congress held in Rio de Janeiro in 1952 and recipient of the College Medal in 1950

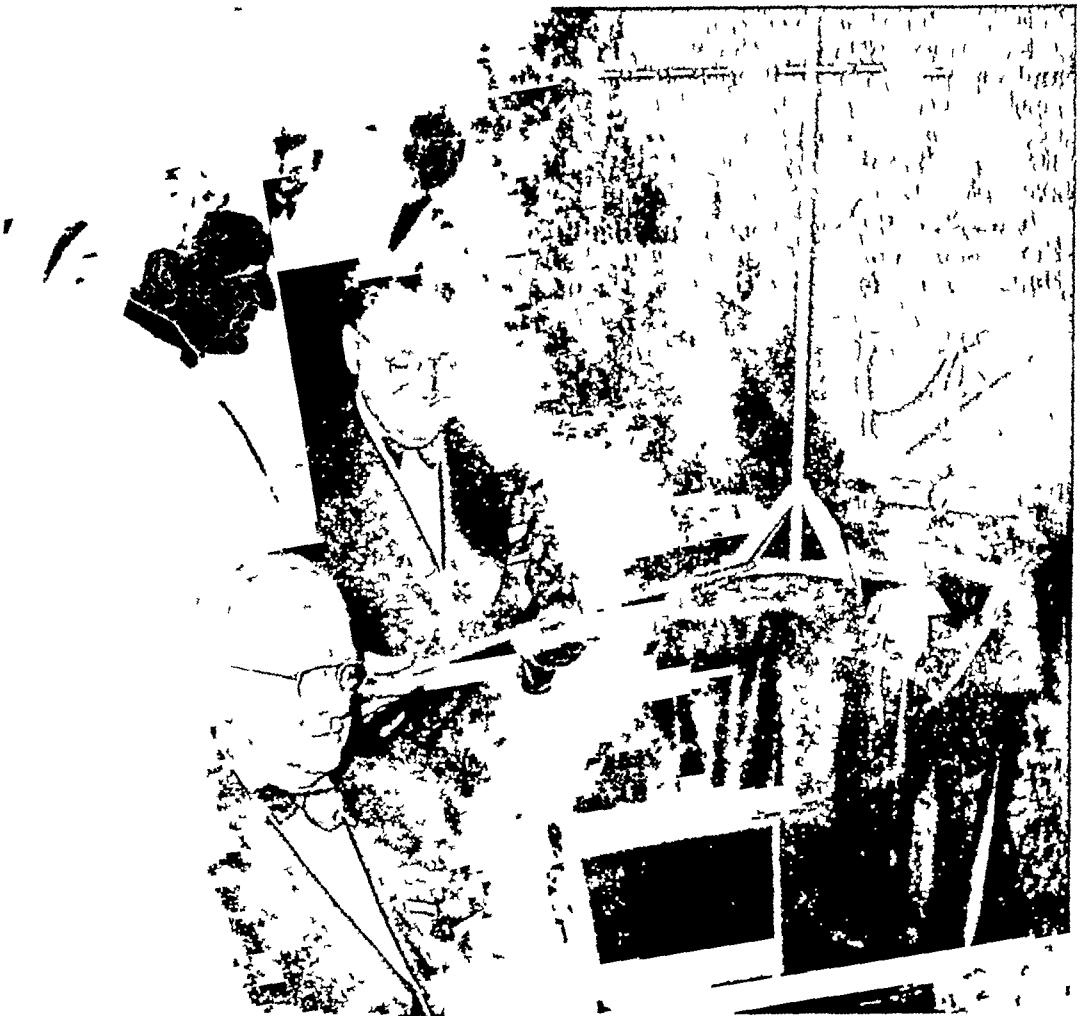
For the convenience of the members of the Congress, postal, telephone, telegraphic, banking, travel and information services, as well as free secretarial assistance were available. Excellent transportation facilities from the hotels to the Palace were provided by the local arrangements committee.

The most popular part of the program were the panel discussions of tuberculosis, tumors of the chest, asthma and emphysema and cardiovascular diseases. The four subjects were presented in the main assembly hall on four consecutive days. Members of these panels, seated at the long speakers' table, were a veritable galaxy of luminaries of medical science. With the help of interpreters and the use of earphones, it was possible to listen to questions and answers simultaneously in five different languages, namely, Spanish, French, German, Italian and English.

Recent advances in the diagnosis, medical and surgical treatment of chest diseases were illustrated in a large number of scientific motion pictures.

More than 250 papers and lectures were presented in five lecture halls. A printed program of 874 pages containing abstracts of these papers translated into the five official languages was presented to each physician regis-

### MURRAY KORNFELD RECEIVES CERTIFICATE



Dr. Luis Rosal, President of the Congress, presenting Mr. Murray Kornfeld with a special certificate of appreciation from the Barcelona Chapter of the College. Seated in foreground, Dr. Burgess L. Gordon, U.S.A., Second Vice President of the College.

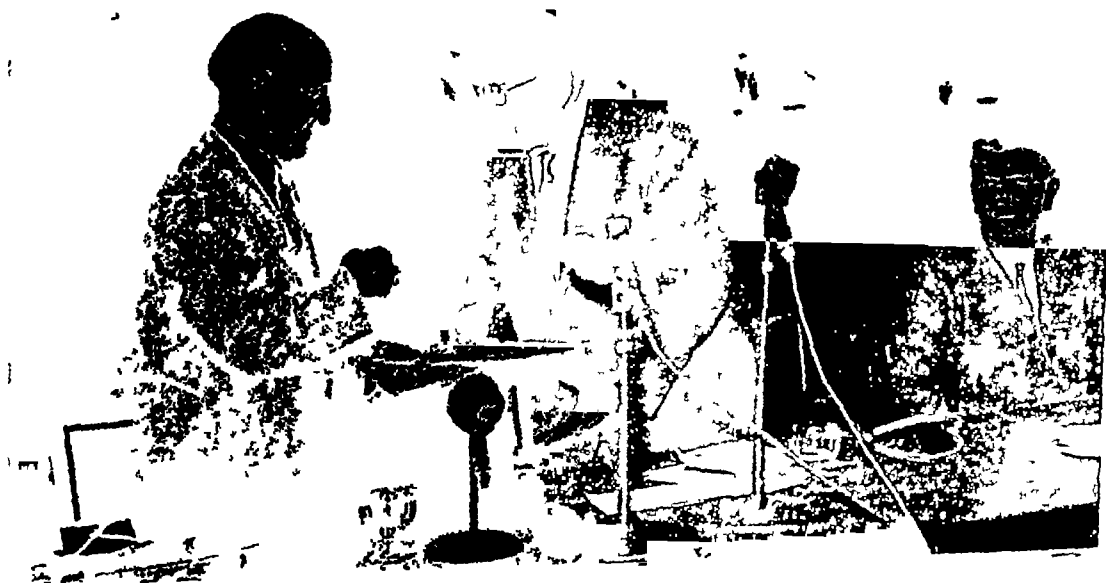
tered for the Congress. The scientific papers encompassed carcinoma and other tumors of the lung, pulmonary infections, parasitic infestations, bronchial asthma, emphysema, cystic disease of the lung, Loeffler's syndrome, foreign bodies, oil granuloma, fibrosis, pneumoconiosis, atelectasis, bronchiectasis, surgery of the thoracic duct and bronchi, diseases of the pleura, diaphragm, mediastinum and esophagus. Several speakers discussed subjects covering cardiovascular diseases. Considerable time was devoted to diagnostic procedures, such as cytology, pneumomediastinum, pneumoangiography, vertical tomograms and others. Experimental and clinical aspects of cardiopulmonary function tests were adequately dealt with.

Moreover, the program included scientific curiosities, such as congenital absence of the hemidiaphragm, retrosternal diaphragmatic hernia, diaphragmatic hernia containing the liver and spleen, a new syndrome called alveolar-capillary block, a new type of pneumoconiosis designated as suberosis (attributable to cork dust), primary melanoma of the mediastinum, simultaneous bilateral spontaneous pneumothorax, essential pulmonary hemosiderosis, agenesis of one lung, Tietze's syndrome, psychogenic pulmonary hemorrhage, bronchopulmonary ossification, regional bronchitis, echinococcus involvement of the myocardium, eosinophilic infiltration of the epididymis, prostate, kidney and muscles in Loeffler's syndrome, the so-called pharyngo-epiglottic syndrome and disappearing giant pulmonary bullae.

Our Spanish hosts were most generous and considerate in entertaining members of the Congress. Senor Simarro, the Mayor of Barcelona, arranged a splendid reception at the "Pueblo Espanol" where the delegates, their wives and guests, were treated to a presentation of typical Spanish dances with the performers dressed in ancient costumes of deep, vivid colors. The high-light of the dancing program was the presentation of "Carmen" by a group of outstanding Spanish dancers which was given in the second portion of the program following a lavish buffet supper.

The splendid social program included a "Bull Fight Fiesta" to which all of the members of the Congress and their guests were invited. In addition, receptions were offered by the officials of the Town Hall and by the deputies for

## DR. LOEFFLER RECEIVES HONORARY FELLOWSHIP



Dr. Wilhelm Loeffler, Zurich, Switzerland (right), receiving certificate of Honorary Fellowship in the College from the President, Dr. Hudson. At extreme right, Dr. Arthur M. Olsen, Rochester, Governor of the College for Minnesota.

the Province. There were also sightseeing tours of the city including a visit to the old Gothic Quarter and to the Maies Museum.

The Congress was closed with a festive banquet given in honor of the participants. It was a spirited, gala event of exquisite elegance, marvelous splendor and unforgettable beauty. Those who sauntered to the spacious balconies of the palace were enchanted by the sight of a huge, running, illuminated fountain below. Its multicolored streams changed their pattern as well as their hue every few minutes, gracefully swaying, pirouetting in lilting curves, embracing and unfolding arches, like a delightful tropical flower or the gorgeous plumes of a giant peacock.

Spectacular as this sight was, it dwarfed next to the intangible values represented by the scientific contributions brought together at this Congress. They were concrete facts from the efforts of great minds, seasoned with the essence of intellect, wisdom and wit.

In view of all this, I am certain the entire membership of the College owes endless thanks and gratitude to our Spanish colleagues, particularly to Drs. Rosal and Carals, the Marquis de Villaverde, Dr. Coll and to all others concerned, for their charming, congenial hospitality and for making this Congress possible.

The narrative of the Congress would not be complete without relating the distinction extended to Murray Koinfeld, Executive Director of the College. In recognition of his faithful, untiring devotion and invaluable services to this organization, he was awarded testimonial plaques of merit by the Spanish, German, Greek, Italian and Portuguese Chapters at the Inaugural Ceremony.

### SCIENTIFIC SESSIONS



The use of earphones for simultaneous translation at the scientific sessions of the Third International Congress on Diseases of the Chest



The Third International Congress on Diseases of the Chest is recorded by this reporter as a memorable tribute to the men whose ability and talent have been guiding the phenomenal growth of this scientific society. May its tremendous success serve forever as an inspiration for still greater achievements.

ANDREW L. BANYAI, M D , F C C P , Chairman  
Council on International Affairs

## Executive Sessions

The Council on International Affairs of the College held two executive sessions during the Third International Congress on Diseases of the Chest. The Inaugural Executive Session, attended by 107 officials of the College, was held on Monday afternoon, October 4, at the Avenida Palace Hotel, Barcelona. Dr. William A. Hudson, President of the College, presided at the session and introduced Dr. Luis Rosal, President of the Congress, and Dr. Antonio Caralps, the Secretary General, who addressed the assembled delegates briefly.

The following reports were presented

*Council on International Affairs*

Andrew L. Banyai, Milwaukee, Wisconsin, U S A , Chairman

*Council on Pan American Affairs*

*North and Central America* John F. Briggs, St. Paul, Minnesota, U S A

*South America* Gumeisindo Sayago, Cordoba, Argentina

*Council on European Affairs*

Attilio Omodei Zorini, Rome, Italy, Chairman

*Council on Pan Pacific Affairs*

Manuel Quisumbing, Manila, Philippine Islands

*Council on African and Eastern Affairs*

David P. Marais, Cape Town, South Africa, Chairman

*Committee on Membership*

Chevalier L. Jackson, Philadelphia, Pennsylvania, U S A , Chairman

*Board of Examiners*

Harold G. Trimble, Oakland, California, U S A , Chairman

*Committee on College Essay Awards*

Richard R. Trail, London, England

*Committee on Resident Fellowships*

Alfred A. Richman, New York, N Y , U S A , Chairman

*Committee on Motion Pictures*

Alfred Goldman, Los Angeles, California, U S A

The reports were received with great interest and discussion followed concerning future activities of the College.

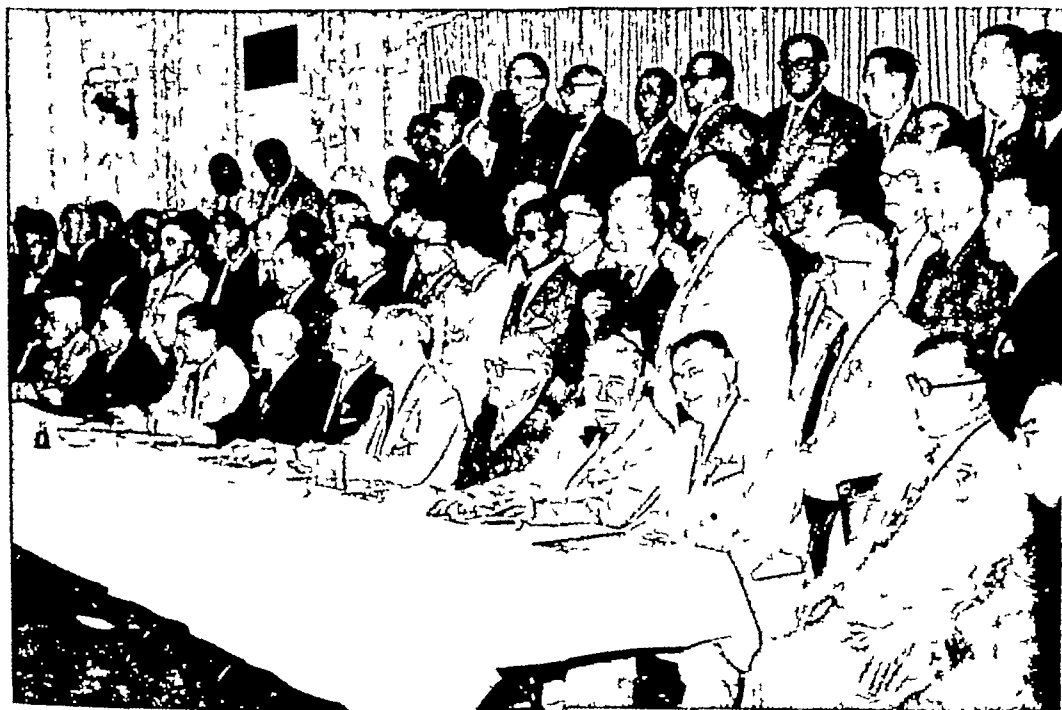
The Closing Executive Session was held on the afternoon of Friday, October 8, at the Avenida Palace Hotel. Dr. Hudson, President, presided. Dr. Antonio Caralps presented the report of the Secretary General of the Congress and expressed the hope of their executive committee that the delegates were pleased with the arrangements of the Third International Congress, now nearing its close. Dr. Hudson extended the profound gratitude of the officers and members of the College to Dr. Rosal, Dr. Caralps and the members of the organizing committee for their splendid work in arranging and conducting this great Congress. Mr. Murray Kornfeld, the Executive Director of the College, expressed his appreciation for the Certificates of Merit presented to him by the Spanish, German, Greek, Italian and Portuguese Chapters of the College.

A resolution was adopted at the Closing Executive Session of the Congress extending the appreciation of the American College of Chest Physicians to Generalissimo Francisco Franco Bahamonde and to all of the officials of the Government of Spain, as well as to the officials of the city of Barcelona and the Province, for their support of the Third International Congress on Diseases of the Chest. Through their cooperation and assistance important scientists from all parts of the world were brought together in Barcelona for the purpose of discussing the most recent developments in the specialty of diseases of the chest. A special vote of thanks was given to Mrs Maluquer-Wahl, Mr Garcia and their assistants, for the excellent manner in which the many details connected with the Secretariat were handled. A vote of appreciation was extended to the scientific and technical exhibitors and special awards were presented to the technical exhibitors for their splendid support of the Congress.

Dr Andrew L Banyai, Chairman of the Council on International Affairs, announced that invitations had been received from six countries for the Fourth International Congress on Diseases of the Chest to be held in 1956. Invitations were received from Austria, Canada, Colombia, Germany, India and the United States of America. The Executive Council of the College, after careful deliberation, accepted the invitation received from the German Republic. Dr Banyai further announced that the city in which the Congress would be held in 1956 had not yet been selected, but that it had been arranged for the Executive Director of the College to travel to Germany immediately following the close of the Congress in Barcelona, in order to inspect the facilities of the various cities. Dr Joachim Hein, Schleswig-Holstein, Regent of the College for Germany, expressed for the German members their pleasure in being selected host for the next International Congress.

The Committee on Nominations, under the chairmanship of Dr Buigess L Gordon, U S A, presented the following slate of officers for election.

### INAUGURAL EXECUTIVE SESSION



Some of the Officials of the College in attendance at the Inaugural Executive Session, Monday, October 4, 1954, Avenida Palace Hotel, Barcelona, Spain

## Regents

*Honorary Regents*

Brazil	Afonso MacDowell	Rio de Janeiro
Canada	William E Ogden	Toronto
Italy	Eugenio Morelli	Rome
Switzerland	Gustav Maurer	Zurich

*Regents*

Argentina	Gumersindo Sayago	Cordoba
Australia	W Cotter Harvey	Sydney
Belgium	Lucien Brull	Liege
Brazil	Manoel de Abreu	Rio de Janeiro
Canada	Harold I Kinsey	Toronto
Central America	Amadeo Vicente Mastellari	Panama City
Chile	Hector Orrego Puelma	Santiago
Colombia	Carlos Arboleda Diaz	Bogota
Cuba	Antonio Navarrete	Havana
Ecuador	Juan Tamen Marengo	Guayaquil
France	Etienne Bernard	Paris
Germany	Jonachim Hein	Schleswig-Holstein
Great Britain	Alexander Fleming	London
Greece	Nicholas Oekonomopoulos	Athens
India	Raman Viswanathan	New Delhi
Italy	A Omodei Zorini	Rome
Japan	Jo Ono	Tokyo
Mexico	Donato G Alarcon	Mexico City
Netherlands	L D Eerland	Groningen
Peru	Ovidio Garcia-Rosell	Lima
Philippine Islands	Miguel Canizares	Manila
Portugal	Lopo de Carvalho	Lisbon
South Africa	David P Marais	Cape Town
Spain	Antonio Crespo Alvarez	Madrid
Sweden	Clarence Crafoord	Stockholm
Switzerland	Wilhelm Loeffler	Zurich
Uruguay	Fernando D Gomez	Montevideo
Venezuela	Jose Ignacio Baldo	Caracas

*Honorary Governor*

Italy	Maurizio Ascoli	Palermo
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*Governors*

Argentina	Raul F Vaccarezza	Buenos Aires
Australia		Sydney
New South Wales	G Bruce White	Adelaide
South Australia	Darcy R W Cowan	Melbourne
Victoria	Alan H Penington	Innsbruck
	Erhard F Kux	Brussels
Austria	Henry Durieu	
Belgium		Salvador
Brazil	Jose Silveira	Belo Horizonte
Bahia	Orlando Cabral Motta	Para
Minas Gerais	Epilogo de Campos	Recife
Para	Joaquim Cavalcanti	Rio de Janeiro
Pernambuco	Reginaldo Fernandes	Porto Alegre
Rio de Janeiro	Carlos Bento	Sao Paulo
Rio Grande do Sul	Jose Rosemberg	
Sao Paulo		
Canada	W Elliott Harrison	Vancouver
British Columbia	J J Quinlan	Kentville, N S
Eastern Provinces	Hugo T Ewart	Hamilton
Ontario	B Guy Beglin	Montreal
Quebec	Leslie Mullen	Calgary, Alberta
Western Provinces	George E Ranawake	Colombo
Ceylon		Concepcion
Chile	Ildefonso Garretton Unda	Santiago
Concepcion	Armando Alonso Vial	Valparaiso
Santiago	Gilbert V Zamorano	Hong Kong
Valparaiso	Li Shu-Fan	Medellin
China	Rafael J Mejia	San Jose
Colombia	Raul Blanco Cervantes	Havana
Costa Rica	Teodosio Valledor	
Cuba		

Czechoslovakia	Jaroslav Jedlicka	Prague
Denmark	Kjeld Torning	Copenhagen
Dominican Republic	J M Moscoso Cordero	Trujillo
Eastern Pakistan	Mohammed Ibrahim	Dacca
Ecuador	Jorge A Higgins	Guayaquil
Egypt	Abdel-Aziz Sami	Cairo
El Salvador	Jose Francisco Valiente	San Salvador
England		
Greater London	Richard R Trall	London
Northern England	Peter W Edwards	Shropshire
Finland	P E A Nylander	Helsinki
France		
Bordeaux	F Piechaud	Bordeaux
Lyon	Paul Santy	Lyon
Nantes	Paul Veran	Nantes
Paris	Maurice Bariety	Paris
Paris	Andre Meyer	Paris
Strasbourg	Eugene Vaucher	Strasbourg
Germany		
Cologne	H W Knipping	Cologne
Freiburg	Ludwig Heilmeyer	Freiburg
Munich	K Bingold	Munich
West Berlin	Walter Unverricht	West Berlin
Wiesbaden	Hans Wurm	Wiesbaden
Greece	Basil Papanicolaou	Athens
Haiti	Louis Roy	Port-au-Prince
Honduras	Ramon Larios	Tegucigalpa
India		
Eastern India	P K Ghosh	Calcutta
Northern India	K L Wig	Punjab
Southern India	K S Sanjivi	Madras
Western India	Prag Nath Kapur	Delhi
Ireland	Victor M. Synge	Dublin
Israel	Juda M Pauzner	Petach Tikva
Italy		
Milan	Giuseppe Daddi	Milan
Naples	Vincenzo Monaldi	Naples
Palermo	Nicola Sanguigno	Palermo
Rome	Giovanni L Eltore	Rome
Japan	Hidejuro Haruki	Tokyo
Korea	In Sung Kwak	Seoul
Lebanon	Papken S Muqrdochian	Beirut
Mexico	Miguel Jimenez Sanchez	Mexico
Netherlands	M R. H van den Berg	Amsterdam
Nicaragua	Rene Vargas	Managua
Norway	Carl B Semb	Oslo
Panama	Augustin A Sosa	Panama City
Paraguay	Juan Max Boettner	Asuncion
Peru	Maximo Espinoza Galarza	Lima
Philippine Islands	Manuel Quisumbing Sr	San Pablo
Portugal	Carlos Alberto Vidal	Lisbon
Scotland	Robert Y Keers	Aberdeenshire
South Africa		
Northern States	Maurice A Pringle	Transvaal
Southern States	Theodore Schrire	Cape Town
Spain		
Barcelona	Luis Rosal	Barcelona
Bilbao	Carmelo Gil Turner	Bilbao
La Coruna	Alvaro Urgoitia	La Coruna
Madrid	Jose Abello	Madrid
Sweden		
Gothenburg	Gosta Birath	Gothenburg
Malmo	Helge B Wulff	Malmo
Uppsala	Erik Hedvall	Uppsala
Switzerland		
Central Switzerland	Alfred Brunner	Zurich
West Switzerland	Maurice Gilbert	Geneva
Turkey	Tevfik Saglam	Istanbul
Uruguay	Armando Sarno	Montevideo
Venezuela		
Caracas	Julio Criollo Rivas	Caracas
Maracaibo	Pedro M Iturbe	Maracaibo
Yugoslavia	Robert T Neubauer	Sezana-Slovenija

The slate of officers as presented by the Committee on Nominations, upon motion from the floor, was duly elected

## EXECUTIVE COMMITTEE

## Third International Congress on Diseases of the Chest

*President* DR LUIS ROSAL*Vice President* DR CRISTOBAL MARTINEZ BORDIU*Secretary General* DR ANTONIO CARALPS*Treasurer* DR. FRANCISCO COLL COLOME

DR A AMELL SANS  
 DR E BILTO REIMAN  
 DR A CASTELLA ESCABROS  
 DR J CORNUDELLA CAPDEVILA  
 DR J CIVIL INGLES  
 DR M GONZALEZ RIBAS  
 DR P GRANENA FIGUET  
 DR RAIMUNDO FROUCHTMAN  
 DR G MANRESA FORMOSA  
 DR F MARGARIT TRAVERSAC

DR J ORIOL ANGUERA  
 DR J PALOU LLAUDET  
 DR A PURSELL MENGUEZ  
 DR J REVENTOS BORDOY  
 DR JUAN BTA ROSET COLL  
 DR J SANGLAS CASANOVAS  
 DR LUIS SAYE  
 DR T SEIX MIRALTA  
 DR J TURELL GUMA  
 DR C XALABARDER PUIG

## INTERNATIONAL COMMITTEE ON BCG

A meeting of the International Committee on BCG was held on Wednesday, October 6, at the Hospital Santa Cruz y San Pablo, Barcelona, Spain, at the time of the Third International Congress on Diseases of the Chest. In the absence of the Chairman, Dr Robert J Anderson, Washington, D C, the meeting was presided over by Dr Gumeisindo Sayago, Cordoba, Argentina, the Vice-Chairman of the Committee. Members of the Committee present at the meeting were Drs Erik Hedvall, Sweden, Andre Meyer, France, and Luis Saye, Spain. The meeting was attended by more than 100 interested physicians from various countries throughout the world.

The agenda for the meeting was as follows

- 1) Vaccines
  - a) Fresh and dried

## BCG CONFERENCE



Physicians attending the BCG Conference held in Barcelona on Wednesday, October 6, 1954

- b) Production
- c) Standardization
- d) Control testing
- 2) Methods
  - a) Preliminary testing, obligatory or not
  - b) Vaccination intradermal, percutaneous, oral
  - c) Post testing
- 3) Effectiveness

At this session, Dr Arnaldo Coro, Havana, Cuba, presented to Dr Luis Saye the Finlay Medal from the Government of Cuba, for his outstanding contributions to medical science

#### FOURTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST

Upon invitation extended by the West German Republic at the time of the Third International Congress on Diseases of the Chest, held in Barcelona, Spain, October 4-8, 1954, the American College of Chest Physicians is pleased to announce that the Fourth International Congress will be held in that country in 1956

Mr Murray Kornfeld, the Executive Director of the College, traveled through Germany after the close of the Congress in Barcelona, and with the assistance of the Regent and Governors of the College in Germany, was able to fully inspect the convention facilities of each of the major cities in that country. A report of his visit to Germany was presented to the Board of Regents of the College at its semi-annual meeting held in Miami Beach, Florida, on November 29, and at that time it was unanimously agreed that



The German Officials meeting with officers of the College in Barcelona. Left to right: Dr Ludwig Heilmeyer, Governor for Freiburg, Dr H W Knipping, Governor for Cologne, Dr Walter Unverricht, Governor for West Berlin, Dr William A Hudson, President, Dr Joachim Hein, Schleswig-Holstein, Regent for Germany, Dr Andrew L Banyai, Chairman, Council on International Affairs, Dr Hans Wurm, Governor for Wiesbaden, and Mr Murray Kornfeld, Executive Director

the City of Cologne, Germany, was best suited for the site of the 1956 International Congress. It is also planned for the delegates to visit many of the other cities in Germany which have extended invitations.

The organization of the Fourth International Congress on Diseases of the Chest will be supervised by an executive committee comprised of the Regent and the five Governors of the College for Germany. The committee members, whose names are as follows, have pledged their complete cooperation and support in the organization of the Congress.

Joachim Hein, Schleswig-Holstein (Regent), Chairman  
Konrad Bingold, Munich  
Ludwig Heilmeyer, Freiburg  
H. W. Knipping, Cologne  
Walter Unverricht, West Berlin  
Hans Wurm, Wiesbaden

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### RECEPTION GIVEN IN MADRID

Dr. Antonio Ciespo Alvarez, Regent of the College, Dr. Jose Abello Pascual, Governor, and the Marquis de Villaverde, Vice President of the Barcelona Congress, gave a reception at the Wellington Hotel, Madrid on September 30, for College members visiting the capital city of Spain. The traditional "copa de vino español," which is the symbol of good fellowship, was the theme of the gathering. Each guest was presented with an album of photographs taken at the reception.



Dr. Cristobal Martinez Bordiu, the Marquis de Villaverde, Vice President of the Third International Congress on Diseases of the Chest, talking with Dr. Jose Abello, Governor of the College for Madrid, and Mr. Murray Kornfeld, Executive Director, at the reception given at the Wellington Hotel, Madrid.

# College Chapter News

## NEW YORK CHAPTER

The annual Clinical Session of the New York Chapter will be held at the Hotel New Yorker, New York City, February 17, 1955. The following program will be presented

- 9 00 a m "Justified and Unjustified Changes in the Treatment of Tuberculosis During the Age of Chemotherapy"  
Robert G Bloch, M D  
"Idiopathic Pulmonary Fibrosis and Related Conditions"  
Louis E Siltzbach, M D  
"Treatment of Bullae of the Lungs"  
William A Zavod, M D  
"Use of Intermittent Positive Pressure in the Treatment of Chronic Pulmonary Emphysema"  
A L Loomis Bell, Jr, M D  
"Some Effect of Diamox on Gas Exchange in Chronic Pulmonary Diseases"  
Daniel S Lukas, M D
- 12 00 noon Luncheon Meeting  
"A Psychiatrist Considers the Chest Patient"  
Alexander Reid Martin, M D
- 2 00 p m Clinical-Pathologic Conference  
Chairman Arthur Q Penta, M D  
Panel Robert L Yeager, M D, Leonard J Bristol, M D, and Marvin Kuschner, M D  
"Subphrenic Abscess—Differential Diagnosis and Treatment"  
Charles B Ripstein, M D  
"Some Clinical Applications of Angiocardiography and Cardiac Catheterization"  
Irving G Kroop, M D  
"Displacements of the Barium-filled Esophagus by Cardiovascular Lesions"  
Nathaniel E Reich, M D, and David E Ehrlich, M D

A five minute question period will be allotted to each topic after the speaker has completed his presentation

## PACIFIC NORTHWEST CHAPTER

The following officers were elected at the annual meeting of the Pacific Northwest Chapter, held in Portland, Oregon, November 12

<i>President</i>	Herbert S Stalker, Vancouver, British Columbia
<i>Vice-President</i>	Norman Arcese, Seattle, Washington
<i>Secretary-Treasurer</i>	William G Trapp, Vancouver, British Columbia

## NEW ENGLAND CHAPTER

Listed below are the dates and programs for the forthcoming monthly meetings of the New England Chapter. Meetings are held at the New England Deaconess Hospital, Boston

January 19 — 4 00 p m

"Modern Concepts in Treatment of Pulmonary Tuberculosis"

Roger S Mitchell, M D

February 16 — 4 00 p m

"The Place of Physiological Studies in Pulmonary Tuberculosis"

Giles Filley, M D

March 16 — 4 00 p m

"Pathology of Tuberculosis Before and After the Era of Chemotherapy"

Oscar Auerbach, M D

April 20 — 4.00 p m

"Clinical Implications of Anomalies of the Pulmonary Circulation"

Irving M Madoff, M D



## ILLINOIS CHAPTER

A joint meeting of the Illinois Chapter of the College and the Chicago Tuberculosis Society will be held on Friday evening, January 28, at the St Clair Hotel, Chicago. The guest speaker will be Professor L. D. Eerland, Chief of the Department of Thoracic Surgery at the University of Groningen, Groningen, The Netherlands. The title of Professor Eerland's presentation is "Surgical Resection in Pulmonary Tuberculosis, Review of 1000 Cases." There will be a fellowship hour at 6:30 p.m. to be followed by dinner and the scientific session.

## BARCELONA CHAPTER

The Barcelona (Spain) Chapter met on November 16, 1954 and elected the following officers:

*President*

Jose Cornudella Capdevila

*Secretary*

Raimundo Frouchtman

*Treasurer*

Francisco Coll Colome

## ARGENTINE CHAPTER

The Argentine Chapter held its annual meeting in Rosario, December 11-12, at which time the following officers were elected:

*President*

Juan B. Rocca, Cordoba

*Vice President*

Francisco Arambarri, Eva Peron

*Secretary-Treasurer*

Jose Antonio Perez, Cordoba

## QUEBEC CHAPTER

The Quebec Chapter recently sponsored a joint meeting of the Montreal Medico-Chirurgical Society and the Societe de Phtisiologie de Quebec at the Royal Edward Laurentian Hospital, Ste. Agathe-des-Monts, Quebec. Members of the College who presented papers at the meeting are: Doctors Roger Lachance, Maurice Doray, Ruben Lauzier, M. Allan Hickey, Philip Edwards, George Lenis, Basil Cuddihy, and J. F. Meakins.

## MOTION PICTURE SESSION ON DISEASES OF THE CHEST

Physicians having new motion pictures on diseases of the chest are invited to send their films for review by the Committee on Motion Pictures of the American College of Chest Physicians for official approval and for consideration for showing at the motion picture session to be held in connection with the 21st Annual Meeting of the College in Atlantic City, June 2-5, 1955. Film data blanks may be secured upon request. Please address films and inquiries to Dr. Paul H. Holinger, Chairman, Committee on Motion Pictures, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois. Other members of the committee are: Houck E. Bolton, Philadelphia, Pennsylvania; Alfred Goldman, Los Angeles, California; H. Corwin Hinshaw, San Francisco, California; David H. Waterman, Knoxville, Tennessee; and Francis M. Woods, Brookline, Massachusetts.

## NEWS NOTES

Dr. Roberts Davies, formerly of Seattle, Washington, has been appointed Director of the Florida State Tuberculosis Board.

Dr. Harold A. Lyons, Brooklyn, New York, recently lectured on "Differential Diagnosis of Chest Disease" at the Symposium on Chronic Pulmonary Disease for General Practitioners.

## 1955 Prize Essay Contest

The American College of Chest Physicians will offer three cash awards for the best essays written on any phase relating to the diagnosis and treatment of chest diseases (heart and/or lungs). First prize will be \$250, Second prize, \$100, and Third prize, \$50. Each winner will also be awarded a certificate of merit. The contest is open to undergraduate medical students throughout the world. The deadline for receipt of manuscripts is April 10, 1955 and instructions for their preparation are as follows:

- 1) Five copies of the manuscript typewritten in English (double spaced) should be submitted to the Committee on College Essay, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois
- 2) The only means of identification of the author shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside enclosing the name and address of the author
- 3) A letter from the Dean or Chairman of the Department of Medicine or Surgery of the medical school certifying that the author is a student at his school

The Board of Regents has recommended that members of the College affiliated with medical schools be urged to bring the contest to the attention of the student body at their respective schools

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### POSTGRADUATE COURSE ON DISEASES OF THE CHEST

The New Jersey Chapter of the College will sponsor its second postgraduate course on diseases of the chest, designed for the general practitioner, at the Hotel Essex House in Newark on consecutive Wednesday afternoons during March, 1955, namely March 9, 16, 23, and 30. Tuition is \$25. Applications and further information may be obtained from Dr. A. Abram Peckman, 2511 Hudson Boulevard, Jersey City 4, New Jersey, director of the postgraduate course

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### ANNOUNCEMENTS

The 15th Congress on Industrial Health, sponsored by the Council on Industrial Health of the American Medical Association, will be held at the Shoreham Hotel, Washington, D. C., January 25-26, 1955

Dr. Leonard A. Scheele, Surgeon General of the Public Health Service, U. S. Department of Health, Education, and Welfare, announced approval of Federal grants for 972 medical research projects, totaling \$10,275,533, for basic and applied research in many of the major diseases. The grants were approved during recent meetings of the seven National Advisory Councils. Two hundred and eighty-nine of the awards, totaling \$3,079,840, were for new research projects, and 683, totaling \$7,195,693, were for continuation of existing projects.

Successful treatment of cardiospasm with drugs, employing a new "topical anesthetic-spasmolytic" has been reported. The preparation used was an experimental liquid form of the drug Dactil which has been recently made available in capsules by Lakeside Laboratories of Milwaukee, Wisconsin.

The American Medical Association recently awarded a special citation to Smith, Kline and French Laboratories of Philadelphia for "pioneering use of television in bettering the health of the nation." This is the first award ever made by the American Medical Association to a commercial house.

## BOOK REVIEWS

**THE HEART BEAT**, by Aldo A. Luisada, M.D., Chicago, Illinois. Published by Paul B. Hoeber, New York, 1953. Pp. 527. Price, \$12.00.

The purpose of this book is to correlate data concerning the various graphic methods now available for recording the heart beat. Tracings of electrical changes, pulsations, pressures, sounds and other phenomena resulting from cardiovascular action are discussed and their clinical applications in common types of heart disease are considered. By means of excellent organization, clear writing and ample illustrations, Dr. Luisada provides a wealth of easily understandable information on the numerous techniques developed during the past quarter-century to facilitate cardiac diagnosis. The discussion of heart sounds is particularly commendable. Every cardiologist should find "The Heart Beat" a worthwhile addition to his library. As new techniques for cardiac study become available, it is hoped that new editions will be published to keep this valuable reference book up-to-date.

Myron Prinzmetal, M.D.

**A PRACTICE OF THORACIC SURGERY**, by A. L. d'Abreu, M.D. Published by Williams & Wilkins Co., Baltimore, 1953.

This text contains in it most of the forward progressive advances in thoracic and cardiac surgery. It is well printed on excellent paper and very well documented with illustrations.

In its organization there are seven parts. Part I—Anatomical and Physiological Considerations. This section also includes a division on pre- and postoperative care and general operative technique. For those neophytes who would establish a new thoracic surgical service in a hospital, this section would be extremely informative. Part II—The Surgery of Pyogenic Infection—is illustrated with excellent bronchograms, and the newer methods such as decortication for empyema are well described. Part III—Pulmonary Tuberculosis—is worthwhile not only for thoracic surgeons but also for phthisiologists. An excellent perspective of the progress of resection in tuberculosis is stated by such a sentence: "The immediate results of resections are so pleasing to surgeon and patient that the gate into a field of almost limitless extent is invitingly open." The thoroughness with which this part is managed is attested to by such sub-headings: "Lesions more suitable for resection than collapse measures", "Lesions that may be suitable for resection or collapse methods or a combination of both", "Resection for lower lobe cavities", "Emergency resection", "Summary of the indications for resection", etc. Part IV is Neoplasms of the Lung and Trachea. It is interesting to note that for post pneumonectomy, phrenic paralysis and pneumoperitoneum is practiced. In this discussion, Dr. d'Abreu rightfully points out that while many innocent tumors are operated upon, those such as leiomyomas, hamartomas, fibromas and lipomas do not need resection of a whole lung for its removal, and he points up that in cases of doubt as to the innocence of the tumor one should err on the side of the lesser resection rather than the greater. In his discussion of bronchial adenoma, he is inclined to underrate slightly the invasive and malignant qualities of this group of tumors but rightfully prefers surgical resection of the tumor to bronchoscopic removal. Part V is the Surgery of the Mediastinum. A separate chapter is devoted to Mediastinal Tumors. Part VI—Some Miscellaneous Conditions—includes among other things the surgical aspects of pulmonary emphysema and asthma and injuries and penetrating wounds of the chest. Finally there is Part VII—a relatively new part, Thoraco-Abdominal Surgery. This brings the book up to date even including a section on porto-caval anastomosis in the treatment of portal hypertension.

There should be no hesitancy in recommending this book to the practicing thoracic surgeon, the general surgeon interested in thoracic surgery, phthisiologists, cardiologists, and medical students.

The book has 591 pages, an excellent index, and a satisfactory bibliography at the end of each chapter.

Alfred Goldman, M.D.

# DISEASES of the CHEST

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NUMBER 2

## Clinical Experience with Pneumoperitoneum in the Treatment of So-Called Hypertrophic Emphysema\*

ANDREW L BANYAI, MD, FCCP and LEON H HIRSH, MD, FCCP

Milwaukee, Wisconsin

The word "emphysema," taken from the Greek, means inflation. The term pulmonary emphysema has been clarified by so many workers that we are now in a state of utter confusion. To recall a few of the adjectives which have been used to modify pulmonary emphysema we shall mention alveolar, diffuse vesicular, dystrophic, essential, genuine, hypertrophic, hypoxic, idiopathic, and obstructive. It is known as chronic large lung, pulmonary dilatation, pulmonary hypertrophy, and pneumonectasis. We believe PSEUDOHYPERTROPHIC EMPHYSEMA or SO-CALLED HYPERTROPHIC EMPHYSEMA are more descriptive terms, for the increase in the volume of the lung is not due to augmented cellular or tissue structure. On the contrary, there is an extensive degenerative process with loss of elastic fibers and destruction of alveoli.

From a clinical point of view it is well to differentiate between pseudohypertrophic emphysema and senile emphysema. The distinguishing features of these entities were described by one of us<sup>1</sup> in the January 1954 issue of *Diseases Of The Chest*.

With the increasing use of mass chest surveys many patients are recognized with pulmonary emphysema. It is desirable to diagnose the existence of emphysema early for the sooner the treatment is begun the more hopeful is the prognosis. However, it would not be expedient to apply the same kind of therapy to patients with senile and pseudohypertrophic emphysema.

Simple clinical observation is often adequate to diagnose so-called hypertrophic pulmonary emphysema. It occurs predominately in men. It is a slowly progressing disease. These patients become dyspnoeic with slight exertion. Many find dyspnoea relieved with pursed lip expiration. They are cyanotic and are observed to have increased venous pressure by watching the fullness of the jugular veins as well as the arm veins even when in the erect or semirecumbent position.

Many of these patients have clubbed fingers, hippocratic incurvation of the nails, and decreased or absent lunulae of the nails. We described the

\*Presented at the 20th Annual Meeting, American College of Chest Physicians, San Francisco, California, June 17-20, 1954.

occurrence of acroerythrosis and palmar erythema in these patients as well as in others with chronic pulmonary disease<sup>2</sup>

The patient may sit leaning forward with his hands on his knees supporting his shoulders

Most patients suffer some degree of cough depending upon the type and extent of coexisting bronchitis, pulmonary fibrosis, or heart failure

Abdominal pain may result from cardiac decompensation with hepatomegaly or anoxia of the diaphragm which we call "diaphragmatic angina"

Wheezing is common. It results from bronchospasm or inflammatory exudate in the bronchi or both

The antero-posterior diameter of the chest is increased producing the characteristic "barrel chest" configuration. Protrusion of the epigastrium during inspiration is decreased or absent

Teleoroentgenograms should be taken in postero anterior and lateral positions both in inspiration and expiration. The patient should be examined fluoroscopically. One observes

- 1) Enlarged lung fields,
- 2) Increased radiotranslucency of the lung fields,
- 3) Dorsal kyphosis,
- 4) Horizontal position of the ribs,
- 5) Widened intercostal spaces,
- 6) Enlarged anterior and posterior mediastinal spaces,
- 7) Small cardiac silhouette,
- 8) Widened costophrenic sulci,
- 9) Diaphragm low, decreased convexity, or both,
- 10) Diaphragmatic respiratory excursions decreased or absent,
- 11) Fluoroscopically, paradoxical motion of diaphragmatic segments

As a simple office procedure we have found that while a normal individual is able to exhale the entire volume of his inspiratory and expiratory reserve air in two or three seconds, patients with so-called hypertrophic emphysema require eight to 14 seconds to complete this maneuver

To approach the treatment of pulmonary emphysema rationally it will be well to review the alterations in the normal physiological status of the lung. One finds pulmonary insufficiency and circulatory disturbances

In this type of emphysema pulmonary insufficiency is due to destruction of elastic fibers, distention and rupture of many alveoli, compression of bronchioles and alveoli by bullae, downward displacement and loss of function of the diaphragm. Decrease in pulmonary ventilation is aggravated by distention of the chest wall. The function of the normal muscles of inspiration and expiration is diminished. One may observe excessive use of the accessory muscles of inspiration

Pulmonary insufficiency is associated with faulty distribution of inhaled air. The alveolar ducts become dilated and lose their jet-like effect normally imparted to inspired air. With loss of pulmonary elasticity the emphysematous lung is unevenly ventilated. Anatomically intact alveoli with normal capillary blood supply receive only a portion of the air current. Some of the inspired air is deviated to the emphysematous alveoli, blebs, and bullae

Such faulty distribution of inspired air is augmented by spasm of the bronchioles

One cannot hope to restore destroyed alveoli. We believe we are able, however, to improve the function of the alveoli which still retain some elastic fibers and capillaries.

We feel that something is accomplished through the use of the following agents:

Digitalis is prescribed for patients in heart failure.

Aminophyllin is used for its influence on the heart as well as for its broncho-relaxing effect.

An anticholinergic agent is employed. The lung and gut are derived from the same embryonic stem. The bronchi and intestine react in like manner. Diethyl methyl ammonium bromide relaxes bronchospasm. It does not produce the drying effect so common with atropine derivatives.

Of the sympathomimetic drugs we use isopropyl epinephrine either as a sublingual tablet or applied as a nebulum.

When bronchial infections occur it is necessary to institute appropriate antimicrobial therapy without delay.

We have found pneumoperitoneum the most effective procedure to restore the function of the diaphragm and thus to improve pulmonary ventilation in patients with pseudohypertrophic pulmonary emphysema.

Pneumoperitoneum is a simple and safe procedure which can be induced and maintained in an office or clinic. Patients who are very ill may be admitted to a hospital for the initial treatment and the first few refills. It is not unusual for patients to be brought to the treatment room in a wheel chair and find that after the initial pneumoperitoneum they are able to walk away without assistance.

Patients should be examined fluoroscopically before each treatment.

For the initial treatment any site on the anterior wall of the abdomen may be selected. One should avoid areas of previous abdominal surgery. We prefer a location three fingerbreadths below or above and to the left or right of the umbilicus. After the pneumoperitoneum is well established one may use a site over an area of maximum collection of air in the peritoneal cavity. This is determined when the patient is examined fluoroscopically before each refill. Thus a point under the costal arch may be chosen, or if the patient lies on either side, the needle may be inserted above the 11th rib. Great caution must be exercised as the pleura normally reflects at the 10th rib laterally. It is possible that some of the instances of air embolism reported in pneumoperitoneum may be due to accidental puncture of the lung when the low intercostal site is chosen. Dasher, Black, Weiss, and Bogen<sup>3</sup> state that air embolism will be least likely to occur if one selects a site below the umbilicus and preferably in the left lower abdominal quadrant.

We use 1 percent procaine to infiltrate the skin and peritoneum both for the initial and for subsequent treatments. Some patients request that local anesthesia be omitted.

The site selected is prepared with a surgical antiseptic solution, sterile drapes are applied; a 19 gauge two and a half inch, long bevel needle is attached to a three way stopcock. The sterile rubber tube is connected between the three way stopcock and a standard Robinson pneumo apparatus.

The needle is pressed slowly and gently through the abdominal wall perpendicular to the skin surface. As it passes through the tissues one may feel the resistance offered by the layers of the abdominal wall.

When the point of the needle is in the abdominal cavity one must draw back on the piston of the syringe attached to the upper aperture of the three way stopcock, being sure the valve is so placed that the needle and syringe are connected. In this manner one ascertains that the point of the needle is not in a blood vessel. If no blood is obtained, 25 cc of air or less is injected from the pneumo apparatus. The flow of air may be permitted by force of gravity or it may be introduced under low positive pressure. If the point of the needle is not in the peritoneal space but in the abdominal wall, air will flow very slowly and the manometer will indicate a non-oscillating positive pressure of 12 to 24 cm of water. If such is the case the needle is slowly advanced and the above maneuver is repeated. When air is injected into the peritoneal space a moderately low positive pressure will be observed.

We have found it best to introduce 50 cc of air at a time, testing for sudden increase of intraperitoneal pressure as well as drawing back on the piston of the syringe before proceeding with the next introduction of air. We believe this reduces the pain associated with stretching of peritoneum and prevents air embolism.

The total amount of air administered with the initial treatment is 500 to 600 cc.

If the pneumoperitoneum is satisfactory one may elicit tympany over the liver in place of the normal dullness. When the patient rises from the table after the initial treatment he usually notices shoulder pain from pressure of the injected air upon the diaphragm.

Refills of 500 to 600 cc of air are given at weekly intervals.

In our clinic we use a simple modification of the Robinson pneumo apparatus for the administration of pneumoperitoneum. The standard apparatus is supplied with a length of rubber tubing which reaches from the number one flask to the control valves. When air in the number one flask is exhausted it is necessary to reverse the position of the number one and number two flasks and allow the fluid to siphon back into the number two flask.

We replaced the above mentioned tubing with one long enough to reach from the control valves to both flasks in either the elevated or lowered positions. We applied a Luer tubing adapter to the end which connects with the flasks. Thus when the air in the number one flask becomes exhausted we reverse the position of the flasks and change the tubing connection so air is now delivered into the peritoneal space from the number two flask.

This modification offers the following advantages

- 1) It saves the time required to refill the number two flask
- 2) It provides a more logical use of the air filter With the standard apparatus when the number one flask is recharged with air, any foreign matter in room air is deposited on the outside of the filter This may be blown into the peritoneal space when the pneumoperitoneum is given With our modification, since air always flows in one outward direction any foreign matter is caught by the filter and retained in the mesh
- 3) It conserves the energy of the nurse who assists with the treatments

Large amounts of air are necessary to relax the lung when pneumoperitoneum is used for the treatment of pulmonary tuberculosis We have found, however, that relatively small amounts of air are more beneficial in the treatment of emphysema In our early experience we found that the diaphragm became more mobile with small amounts of air When the volume of pneumoperitoneum was increased the diaphragm lost some of its motion Our patients complained of abdominal discomfort and increased dyspnoea when the amount of air exceeded an optimal quantity Beck, Eastlake, and Baiach<sup>4</sup> presented their studies of venous pressure and pneumoperitoneum before this College They showed tracings of venous pressure which was initially elevated, became lower with the introduction of pneumoperitoneum, and again became elevated when the volume of pneumoperitoneum was increased beyond a critical level

The patient is encouraged to wear a well fitting abdominal support In this manner a smaller amount of air may accomplish the desired therapeutic result

We have continued therapeutic pneumoperitoneum for years It is difficult to determine the proper duration of treatment and each patient must be considered individually

One patient discontinued therapy because he suffered an attack of acute appendicitis Following appendectomy and interruption of pneumoperitoneum, his dyspnoea and cyanosis became severe It was necessary to re-establish the treatment two weeks after appendectomy It has been maintained since

Another patient was completely disabled with emphysema With pneumoperitoneum he was able to return to full time employment One night he suffered acute intestinal intussusception requiring emergency surgery Following this surgery the patient continued well without pneumoperitoneum We believe that if sufficient muscle tissue remains in the diaphragm and if diaphragmatic function can be reestablished one may facilitate some muscle eutrophy In such instances patients may be able to abandon pneumoperitoneum after a period of time On the other hand, if the diaphragmatic muscle has suffered such atrophy of disuse that muscle eutrophy does not occur, then pneumoperitoneum may have to be maintained indefinitely

One may anticipate most relief when the entire diaphragm is mobilized We have observed marked symptomatic relief however when one leaf of



the diaphragm remains fixed by adhesions and the other leaf is mobilized with pneumoperitoneum. These patients may complain of abdominal pain due to stretching of adhesions especially after a refill. Such pain is partially relieved by salicylates. Most patients enjoy enough relief of respiratory distress to disregard the abdominal discomfort.

We believe a comment relative to one of our patients is pertinent. He was returned to his family physician from a large clinic with the diagnosis of 1) PULMONARY EMPHYSEMA, and 2) MENTAL DEPRESSION. Psychiatric treatment was recommended. Curiously, one of us arrived to examine him in the hospital at the same time as the psychiatrist. The patient was truly depressed. He was totally disabled. He was about to lose his job. He couldn't walk five feet from his bed to the wash room without dyspnea and cyanosis.

The psychiatrist recommended shock therapy to improve the mental depression. He agreed, however, to postpone it until we could try pneumoperitoneum treatment to improve the pulmonary ventilation.

This is the patient we mentioned before who was able to discontinue pneumoperitoneum treatment after six months of therapy and who now works full time without pneumoperitoneum. It is now a year since he has received pneumoperitoneum. He was examined fluoroscopically a few weeks ago. The diaphragm which had been depressed and immobile with respiration before pneumoperitoneum still retained the mobility which was observed during the therapy.

We should like to submit the brief that therapeutically pulmonary emphysema stands in the relative position today which was occupied by pulmonary tuberculosis 25 years ago. If we can diagnose and treat these patients in the early stages of the disease we believe they will not become the desperate respiratory cripples who are now encountered.

#### CONCLUSIONS

There is no consensus relative to the etiology of pseudohypertrophic pulmonary emphysema. It should be differentiated from other forms of pulmonary emphysema—particularly senile emphysema which is an involutional condition. One of the cardinal features of pseudohypertrophic pulmonary emphysema is the low position of the diaphragm and functional diaphragmatic insufficiency. Artificial pneumoperitoneum aims at restoring the normal anatomic and physiologic status of the diaphragm.

Pneumoperitoneum in itself does not represent the complete management of the patient with emphysema. It is necessary to correct circulatory and bronchial disturbances which are part of the disease.

In our practice this program has been found a safe and useful method of treatment of patients who suffer with emphysema. Its use is followed by gratifying subjective and objective results in the great majority of individuals.

#### RESUMEN

No hay un acuerdo respecto de la etiología del enfisema pulmonar pseudohipertrófico. Este debe diferenciarse de las otras formas del enfisema

pulmonar, en particular el enfisema senil que es una condición de involución. Una de las características cardinales del enfisema-seudohypertrófico es la posición baja del diafragma y la insuficiencia diafragmática. El neumoperitoneo artificial tiende a restaurar la situación anatómica y fisiológica del diafragma.

El neumoperitoneo por sí no representa el tratamiento completo del enfermo con enfisema. Es necesario para corregir los trastornos circulatorios y bronquiales que forman parte de la enfermedad.

En nuestra práctica este plan es encontrado seguro y útil para el tratamiento del enfisema. Su uso es seguido de resultados satisfactorios tanto subjetivos como objetivos en la gran mayoría de los sujetos.

#### RESUME

L'accord général n'est pas fait sur l'étiologie de l'emphysème pulmonaire pseudohypertrophique. Il semble qu'il y ait une différence entre cette forme et les autres catégories d'emphysème pulmonaire, et en particulier l'emphysème sénile, qui représente un caractère involutif. Un des éléments essentiels de l'emphysème pulmonaire pseudohypertrophique est la situation basse du diaphragme et l'insuffisance fonctionnelle de ce muscle. Le but que l'on se propose avec le pneumopéritoine artificiel est précisément la restauration de l'état anatomique et physiologique normal du diaphragme.

Le pneumopéritoine ne représente pas à lui seul tout ce que l'on doit faire pour traiter l'emphysémateux. Il faut de toute nécessité corriger les troubles circulatoires et bronchiques qui représentent une partie de la maladie.

Dans la pratique des auteurs, l'application d'un tel programme a permis des résultats certains et favorables chez les emphysemateux. La conséquence en a été une amélioration subjective et objective pour la grande majorité des malades.

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- 3 Dasher, W. A., Black, J. P. M., Weiss, W. and Bogen, E. "Air Embolism Complicating Pneumoperitoneum: A Review," *Am Rev Tuberc*, 69 396, 1954
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# The Los Angeles X-Ray Survey Film and Record Library, Its Past Development, Present Activities and Future Possibilities

BLANCHE PERKINS\* and EMIL BOGEN, M D, F C C P \*\*

Olive View, California

The nearly 2,000,000 microfilms and 55,000 large films taken during the Los Angeles X-Ray Survey of 1950 together with the records of the data available regarding them constitute a unique mass of source material which is invaluable for both practical and scientific purposes. The \$200,000 contributed by the County Government, and more than \$1,000,000 expended by the Public Health Service and local agencies in this survey, as well as the contribution of time and materials by thousands of citizens have already been more than repaid by the decrease in sickness and death from tuberculosis which has already followed the survey. Still greater harvest, however, remains to be reaped through the maintenance of the library and its continued utilization.

In the absence of long range planning for the preservation and maintenance of the survey films and records, the developing demands for this material were met during and after the completion of the survey by the Survey Foundation and its staff. Then the Los Angeles Tuberculosis and Health Association provided for the cost of continuation of the library, which was moved in May 1952 to the northeast portion of the main floor of the old psychopathic building of the Los Angeles General Hospital, and on July 1, 1953, the entire support of the library was assumed by the County Government, and it is hoped that this arrangement may be continued.

Three monographs, *The Big Picture*, published July 1951, a statistical study, *Report of Confirmatory Chest X-ray Film Findings Indicative of Tuberculosis*, published in June 1952, and *A Statistical Analysis and Review*, by G. J. Drolet in May 1953, have presented the chief findings made available during the survey itself and the immediate follow-up. Many other studies, however, are now under way and may be carried on in the future with this material, which may even be more important.

As a preliminary to the statistical analysis of the survey material, a census tract index of all addresses in the entire county was prepared. Copies of this index have been available to the County Government and are already being utilized in several different departments, some of which, as the Probation Department, had already spent much time and effort in attempting to prepare such an index of their own previously, and in 1954 these census tract indices were utilized in the Interim Census of Los Angeles.

\*Librarian

\*\*Chairman, Medical Research Committee of the Los Angeles Tuberculosis and Health Association

Records of all of the individuals participating in the survey were then assigned to census tracts and tabulation made of the age, sex and race distribution of the positives and negatives for each census tract. Information regarding the incidence of tuberculosis in different areas of the county have been thus made available to the Health Departments. Additional studies of the geographical distribution of the population and of the disease are now under way which may shed further light on where and how case-finding activities should be planned in the future. Thus, for example, it has been shown that an x-ray unit placed in a jail will yield more than 100 times the proportion of cases of tuberculosis than one placed in a high school, and that a unit taking only 100 films a day in some areas of the city would find many more cases than one which took 1000 films a day in another—Main Street or Central Avenue as compared with Beverly Hills or Westwood.

Further studies of ecological mobility, the pattern of travel and tendency to go out of the local neighborhood for the x-ray examination may further increase our knowledge. The scores of different ways in which the county has been divided geographically for various purposes has also been investigated, and the result of this study should constitute a useful contribution to city planning and statistical study of many kinds and even to further governmental boundary fixing.

A duplicate set of records of old films has been arranged alphabetically. Alphabetic arrangement of nearly 2,000,000 cards has represented an investment of approximately \$20,000, or about 1¢ per card, and is one of the largest projects of this kind known, being many times that involved in any available telephone directory or street or city directories known. Now that this alphabetizing has been completed, however, it discloses many facts and makes possible other investigations which were previously not available. Thus the study now under way has shown that over 60,000 people had more than one film taken during the survey, and comparisons of the findings of these repeat films on the same individual have given valuable information regarding the reliability of the readings of the films as well as regarding the development of tuberculosis in short periods of time.

The alphabetic arrangement has also made possible checking the survey population against the newly reported cases of tuberculosis and deaths from tuberculosis in the county. This has shown how often persons who received a negative report in the film in the survey taken in 1950 have since developed the disease and succumbed from it during the first, second or third year which has elapsed since the films were taken. Additional information regarding the misinterpretation of lesions which were present at that time but not recognized on the film should lead to improvement in the examination and interpretation of minifilms in the future.

There are at present nearly as many case-finding units operating in the Los Angeles County as were utilized during the survey, especially in the various hospital admission programs, Health Departments and other agencies, although few of them take anything like as many films

in a day, as were taken during the survey. Improvements in the conduct of these many case-finding units, however, may greatly increase the value, both in finding cases which might otherwise be missed, and also in preventing the arousing of unfounded suspicions.

Extensive clinical material represented by these 2,000,000 films is of great value in a large variety of anthropometric, anatomic and physiologic, as well as medical studies. Thus the 200 instances of dextrocardia in this series, the largest ever made available, have been analyzed from many points of view, and nearly 100 of the persons concerned have voluntarily returned for further x-ray and electrocardiographic study which have shown great light on the origin and especially on the clinical significance of this condition. A study of the age incidence of cases of scoliosis shown in the survey would be of particular orthopedic interest and may aid in the recognition of etiologic factors in this condition. A large number of studies regarding cancer and heart disease have already been presented, and many more are possible on the basis of the material contained in these records.

Originally it was expected that the film library would be required chiefly during and immediately following the survey and thereafter that the films might well be, as done in most other places, distributed to the various health departments or even destroyed. The time which has elapsed since the survey, however, has shown that this would indeed be a tragedy, and would lose some of the greatest potentialities for good in the survey. Every year, the development of new instances of tuberculosis, cancer and heart diseases makes possible further study of the value of the survey in disclosing and predicting the occurrence of such conditions. In fact it may well be expected that the final evaluation of the significance of this great case-finding survey cannot be made before five or 10 years have elapsed to give time for the evaluation of the cases found and of those which have been missed.

The work of the Film Library has shown no sign of decreasing during the past three years since the survey was completed. Every day scores of telephone calls are received and scores of letters from patients, physicians and county and city officials, some of these merely as for general information about the survey or facilities for obtaining an x-ray examination or care of tuberculosis at present, but the majority request specific information as to whether individuals had participated in the survey and what the result of the examination had been. Dozens daily ask for the film itself. More than 12,000 films have been sent out to physicians or Health Departments from the Survey Library since the survey was held. About half of these are the large 14 x 17 films taken in cases where the screening film showed suspicious shadows, though many of these 14 x 17 films were themselves reported as normal. Comparison of the shadow seen on the earlier film with the one present at the time of examination enables the physician to recognize better the nature of the lesion and its activity, as well as its probable course, and so aids in treatment and the management of the case. From the beginning requests were also made

for minifilms in which no lesion had been reported, and such questions have been actually increasing, or at least show no sign of lessening as time goes on. The value to a physician of a previous film in the evaluation of newly discovered density in the lung may be immense, fear of malignancy may be allayed if the density remained unchanged over a long period of time. Inactivity in tuberculous lesions may be similarly confirmed, or the suitability for chemotherapy or surgical therapy shown by the changes between such successive films.

In addition to receiving requests and sending out the films, the librarian sends out letters and lists requesting return of films daily, and dozens of films are received daily in response to such requests. Importance of recovering films by the library is shown by the large number of requests for films which have been already sent out. Several such requests are received daily—and it is only by continuously reminding the physicians or the clinics which borrowed the films to return them that the library is able to function completely. The librarian is also continuously engaged in rechecking and correcting the filing of the various types of materials under her care, seeing that the films are returned to their proper places, that the cards are kept in correct order, and correcting errors which had unavoidably occurred in the past.

THE LOS ANGELES X-RAY SURVEY FILM AND RECORD LIBRARY  
TABLE I

	Total to October 1953	Per Working Day Average 1953
Telephone calls	30,000	24
Letters in	20,000	12
Letters out	1,000	6
(Lists of films comprizing)	12,000	12
Films sent out		
70 mm	10,000	8
14 x 17	10,000	8
Films received		
70 mm	10,000	10
14 x 17	10,000	20
Duplicate reports		6
Requests for films that are out of Library, which are located for doctors and clinics		4

The extensive material represented by the survey of 1950 may be supplemented by the addition of similar material from smaller surveys conducted by other agencies. All of the films and records of the surveys which have been conducted in the past by the Los Angeles County Tuberculosis and Health Association for example have already been received by the Film Library, as well as the duplicate report cards on all admission

minifilms taken at the Los Angeles General Hospital during 1952, the first year of this program. Additional films, particularly the negatives from the surveys conducted by City and County Health Departments, public schools, the various hospitals and other interested agencies in this County are also being added to the archives. Comparison of the findings in cases in such surveys who were included in the County wide survey or other series would yield much further information of value both to the individual concerned and to the evaluation of the efficacy of the various case-finding programs.

### SUMMARY

Tuberculosis had represented a tremendous drain on local governmental agencies, as well as upon the people who support them. The recent decline in tuberculosis morbidity and mortality rates have already greatly lightened the relative burden to the tax-payers from this disease. For some years, however, the continuance of unrecognized cases in the population constitutes a constant menace of the renewed spread of the disease. Maintenance of the X-Ray Survey Film and Record Library constitutes a substantial contribution to the maintenance of the control and the further studies which may accelerate the disappearance of tuberculosis. The utilization of the x-ray film survey in the investigation and control of cancer, heart disease and other conditions detected by chest surveys may then be contemplated.

### RESUMEN

La tuberculosis ha representado un gasto tremendo en el Gobierno así como en las personas que soportan a los enfermos. La declinación reciente de la morbilidad tuberculosa así como la mortalidad, ha aligerado grandemente la carga que esta enfermedad representa sobre los contribuyentes.

Por algunos años sin embargo, la continuación de casos no reconocidos en la población constituye una amenaza de renovada diseminación de la enfermedad. Una contribución importante para el mantenimiento del dominio de la enfermedad, es la prosecución de la búsqueda por los catástrofes radiográficas y el mantenimiento de archivos de seguimiento y los estudios ulteriores pueden acelerar la desaparición de la tuberculosis. La utilización del a investigación por los rayos X en los grandes grupos, para localizar cáncer, afecciones del corazón y otras afecciones por esos métodos, puede preverse.

### RESUME

La tuberculose a représenté un appel de fonds considérable sur les administrations locales aussi bien que sur le public qui l'a subi. La diminution récente de la morbidité et de la mortalité a considérablement allégé le fardeau de ceux qui contribuaient à payer les frais de cette affection. Pendant quelque temps cependant, il continuera à y avoir des cas non diagnostiqués dans la population et ainsi persistera une menace d'une extension nouvelle de la maladie. Il faut persévérer dans les examens radio-

logiques systématiques et dans la mise à jour des archives des malades, qui réalisent une importante contribution à la lutte contre la maladie, et la continuation des recherches scientifiques qui hâteront la disparition de la tuberculose. C'est alors que l'on pourra fixer son attention sur le rôle des examens systématiques dans la recherche et le traitement du cancer, des affections cardiaques et d'autres affections qui peuvent être découvertes par ce procédé.



# The Ballistocardiogram in the Presence of Pulmonary Disease

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The purpose of this study was to determine the value of ballistocardiography in differentiating cardiac from pulmonary pathology in patients with pulmonary tuberculosis. Clinically, the picture is at times not well delineated. Dyspnea and pain occur in both pulmonary and cardiac disease, and the electrocardiogram in many cases of pulmonary disease presents non-specific abnormalities, mostly due to mediastinal shift and rotation.<sup>1</sup> Fluoroscopic or roentgenographic examination is frequently not conclusive due to the indiscernibility of the cardiac contour in the haze of pleuro-pulmonary distortion. It was, therefore, hopefully attempted to look for new avenues of approach to the problem of differential diagnosis.

## *Procedure*

The ballistocardiograms of 100 consecutive patients were analyzed primarily as to form and amplitude of the systolic and diastolic complexes. The apparatus used was the Glennite Ballistocardiograph made by the John Peck Laboratories of New York. Some tracings were obtained under basal conditions. Most tracings, however, were secured about two or three hours after breakfast or after lunch. Only tracings of patients who appeared nonchalant and relaxed were used in this study. All patients had pulmonary tuberculosis in various stages of activity—unilateral or bilateral. Some had unilateral pneumothorax at the time the tracings were obtained. All were ambulatory and none had associated difficulties. None were tachypnoeic or dyspnoeic. Those who seemed not to be able to obey commands of holding breath, etc. were not included in the study. None had evidence of cardio-vascular disease. Simultaneous complete electrocardiograms were obtained in all cases. The age groups were as follows: 63 cases were between the ages of 16 and 40, 20 were in the fifth decade, 17 were 50 years old or older.

## *Results*

In the analysis of our series a patient was considered to have a normal tracing if the normalcy appeared in any phase of respiration—and leniency was generally applied to the interpretation of the normal, based on preliminary experience and anticipation of "more than usual" respiratory variations.

Of the 68 below the age of 50 and without therapeutic pneumothorax, 29 had normal electrocardiograms and normal ballistocardiograms, 24

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From the Cardiac Service of Sea-View Hospital, Staten Island, N. Y.

had normal electrocardiograms and abnormal ballistocardiograms, eight had abnormal electrocardiograms and normal ballistocardiograms. The abnormalities in the electrocardiograms were those seen in mediastinal shift and were not interpreted as indicative of myocardial damage, seven presented abnormal electrocardiograms and abnormal ballistocardiograms. *The total number of abnormal ballistocardiograms in this group was 31.*

There were 15 below the age of 50 with therapeutic pneumothorax. Of this group seven had normal electrocardiograms and normal ballistocardiograms, five had normal electrocardiograms and abnormal ballistocardiograms, one had an abnormal electrocardiogram and a normal ballistocardiogram, in three both the electrocardiogram and the ballistocardiogram were abnormal. Thus, in the combined group of 83 patients below the age of 50—39 (50 per cent) had abnormal ballistocardiograms.

In 15 of the 20 individuals in the fifth decade, the electrocardiogram was normal and the ballistocardiogram was abnormal. In two cases both the electrocardiogram and the ballistocardiogram were abnormal. In two instances the electrocardiogram and the ballistocardiogram were normal and in one case the electrocardiogram was abnormal and the ballistocardiogram was normal. Thus, in the fifth decade group of 20 patients, *only three had normal ballistocardiograms.*

Of the 17 in the older age group (50 plus) none had an abnormal electrocardiogram. Only three had a normal ballistocardiogram. Two of the abnormal tracings were considered to belong to class two (Brown et al).<sup>2</sup> The rest belonged to group three and four (Brown et al).

The heart rate in the majority of the entire group of 100 cases studied varied between 80 and 100 per minute. Twenty had a heart rate of 80 or lower. Nine of this group had abnormal tracings and 11 had normal ballistocardiograms.

### *The Trace*

The following observations were made in the ballistocardiograms of the series studied. In the few cases with tachycardia only L and M waves could be distinguished in the diastolic phase. In many cases in the same strip *marked* fluctuations in the depth of the I wave and amplitude of IJ and JK were frequently encountered. I was frequently shallow in inspiration and occasionally in expiration. JK was frequently seen to be unusually small in inspiration and occasionally notched. K was seen to be frequently deep in both the inspiratory and expiratory phase. The IJ/JK ratio was frequently smaller in inspiration than in expiration. By the same token the total systolic amplitude was frequently smaller in inspiration than in expiration. The diastolic waves were marked by inconstancy in form and amplitude. H and L were frequently markedly exaggerated and variable in the same strip. H was occasionally notched in expiration or inspiration.

On a number of occasions the "resting" tracings were bizarre and assumed a normal configuration in either the inspiratory or expiratory phase.

It was occasionally observed that a tracing was good one day and not definitive the next day, for no apparent reason. Differences in amplitude

and form were obtained in tracings taken in the morning and afternoon of the same day. Some tracings were better immediately after a meal than on an empty stomach. Two tracings presented low amplitude complexes. One for no obvious clinical justification assumed a normal pattern at a later date. She was 36 years old with an abnormal electrocardiogram, interpreted as due to mediastinal displacement and rotation. The other was a 24-year-old female with a low voltage electrocardiogram in the standard leads. The ballistocardiogram in this case presented a systolic amplitude of 4 mm in the resting and inspiration tracing. In expiration the amplitude was only 3 mm. I and K were shallow. I was particularly shallow in inspiration. In seven cases traces were obtained prior to and following establishment of pneumothorax. It appeared that in this small series the H and L which were exaggerated in the pre-pneumothorax

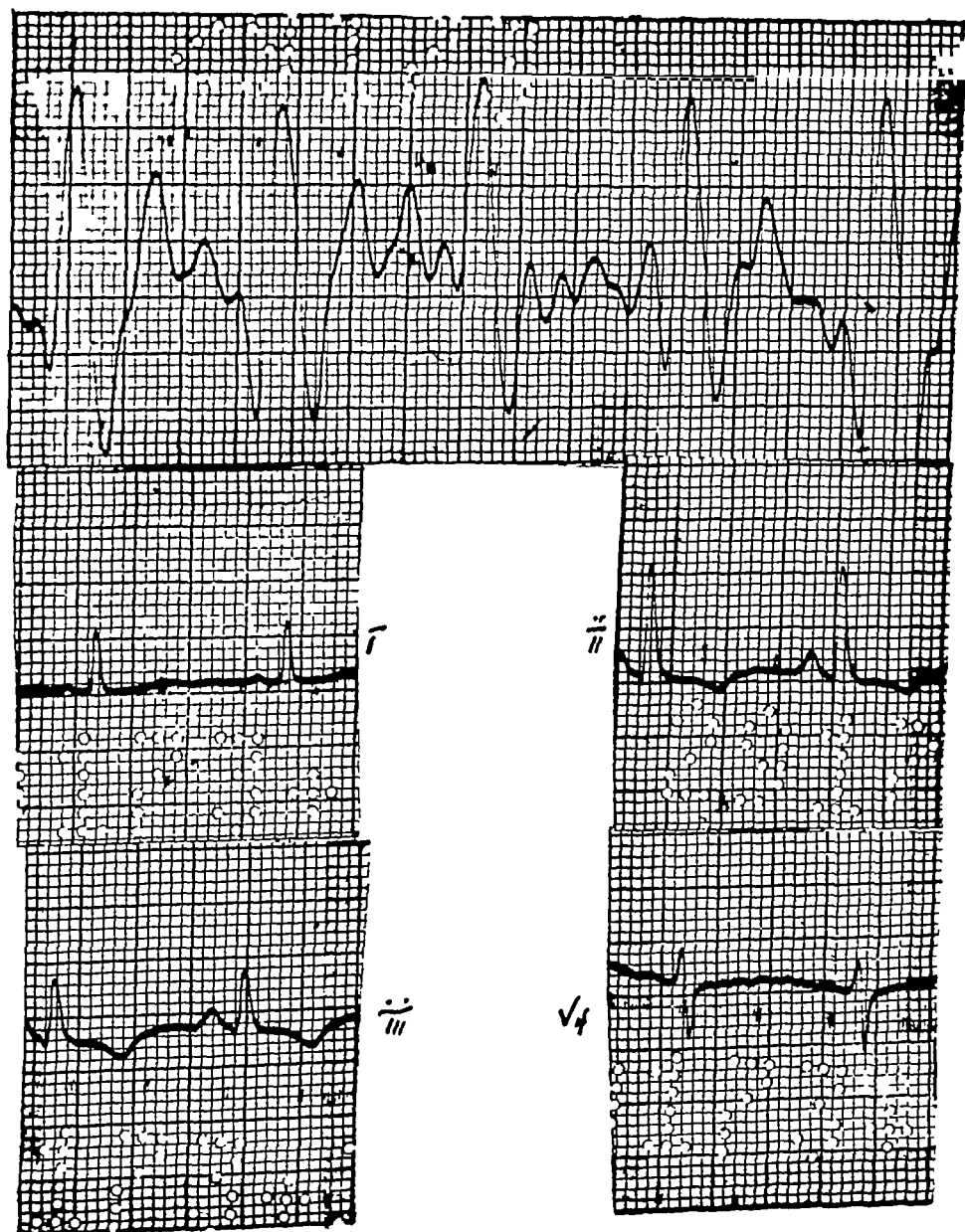


FIGURE 1 Normal ballistocardiogram Abnormal electrocardiogram

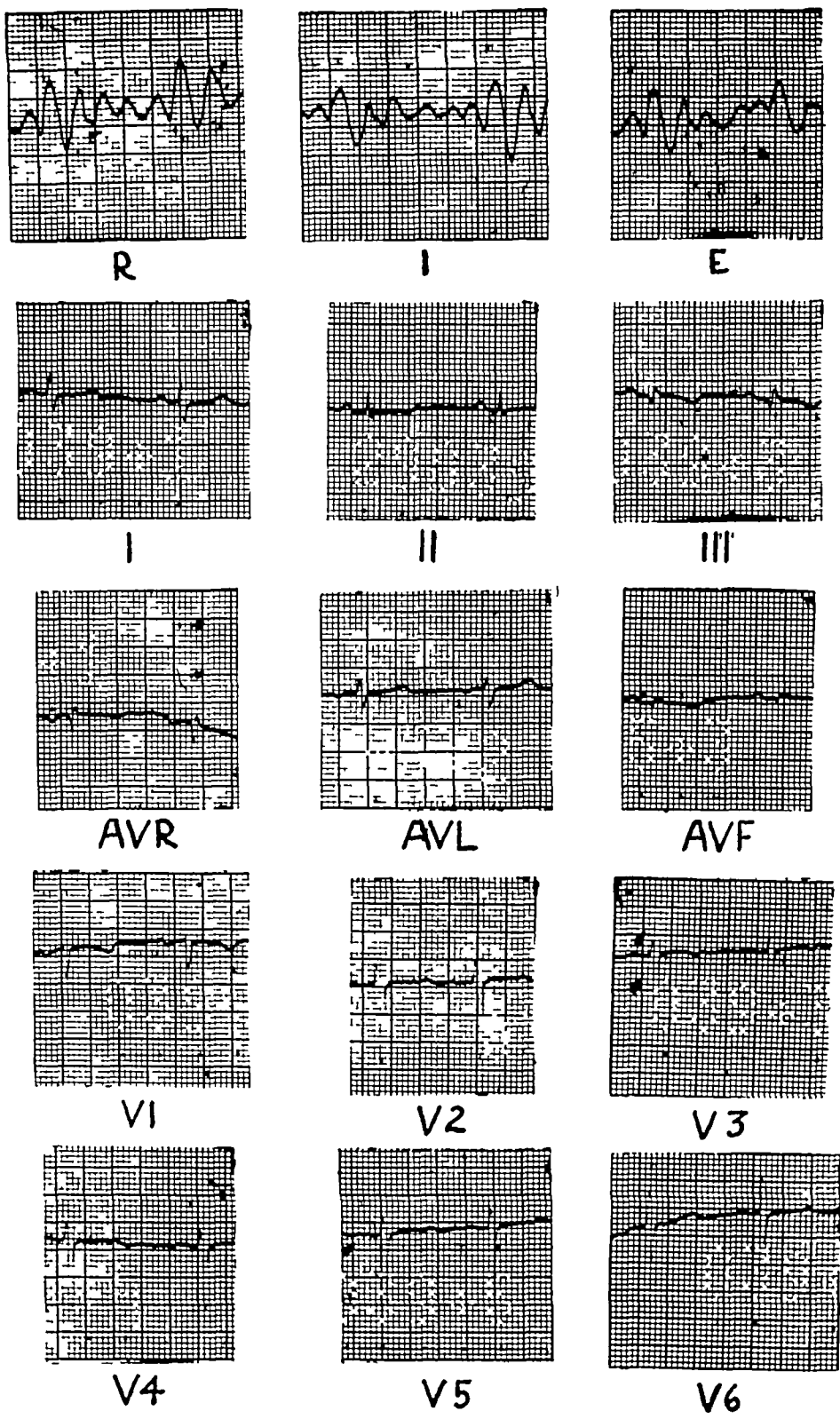
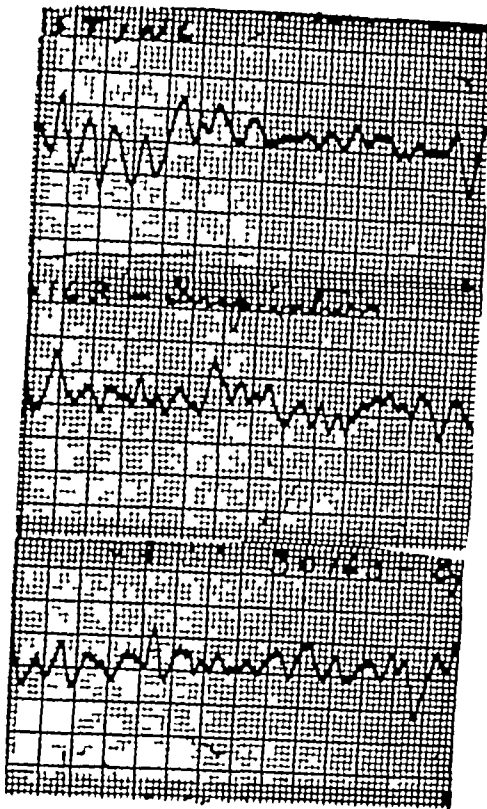
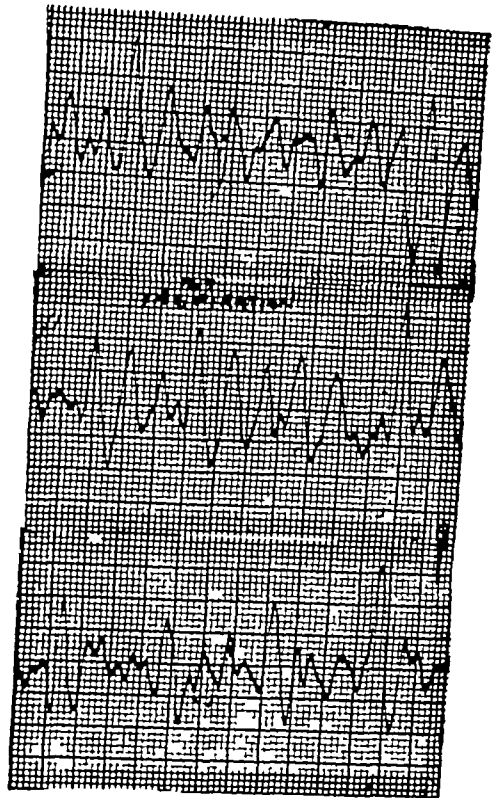


FIGURE 2 Note variations in all respiratory phases Abnormal electrocardiogram

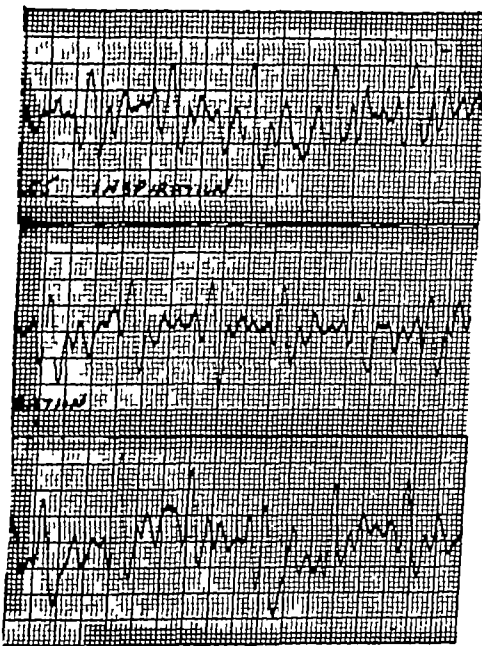


A

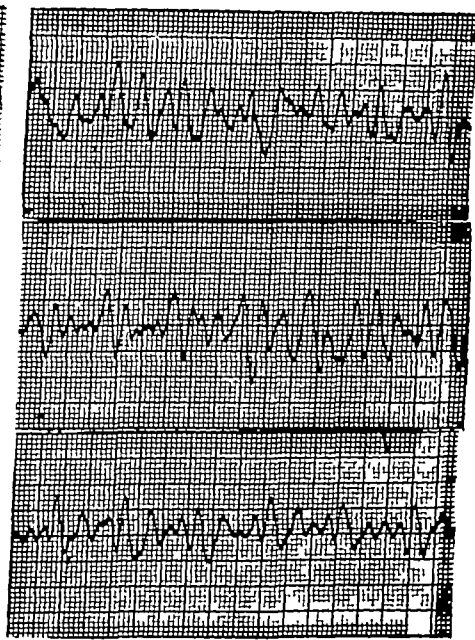


B

*Figure 3A* Ballistocardiogram obtained before breakfast, grossly abnormal—*Figure 3B* Ballistocardiogram obtained shortly after lunch. Note definitiveness in the expiration phase with changes in amplitude of the systolic complex, slurring and notching of IJ and JK



A



B

*Figure 4A* Tracing obtained at 9 A.M. Normal—*Figure 4B* Tracing of same patient at 2 P.M. Note abnormalities with normal respiration (resting), shallow I in the inspiration phase and stability of pattern in the expiration phase

tracings *diminished* in amplitude following institution of pneumothorax. In two the pre-pneumothorax tracings were classified as belonging to group two (Brown et al). Following pneumothorax the tracings were normal—both in the expiration phase only.

### *Positional*

In 31 cases ballistocardiograms were obtained in the prone, right and left lateral positions. It was reasoned that perhaps in some positions and not in others will the respiratory rhythm be more regular and the mechanical interference with respiration will be lessened, and perhaps a change will take place in the intrathoracic dynamics and thus modify the cardiac outflow. It was realized that the lateral position introduces the factor of change in surface contacts. Care was exercised to have the patient in the best possible resting condition and the apparatus was carefully positioned so as to avoid technical errors. Since most of the patients had bilateral pulmonary disease of varying degree, no position could be assumed to be the optimum position. Further studies are now being con-

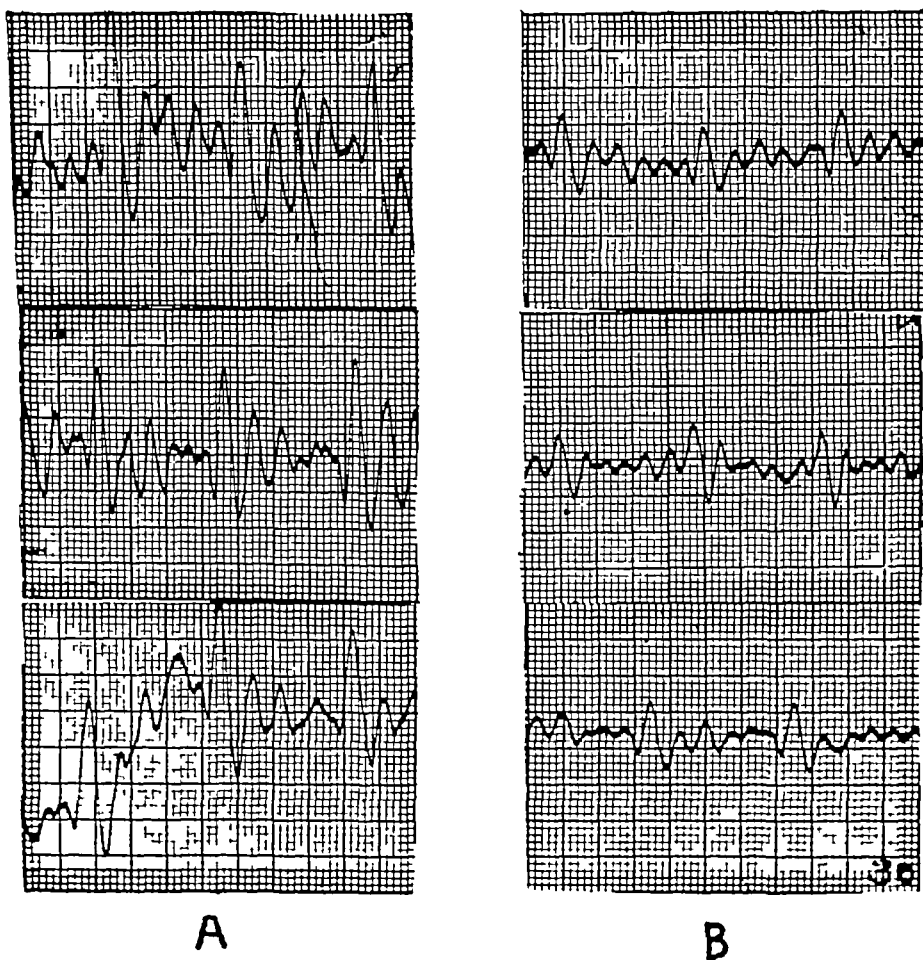


Figure 5A Tracing obtained at 9 A.M., after breakfast—Figure 5B Tracing of same patient obtained at 2 P.M., about 2 hours after lunch. Note change in amplitude. Note shallow I and deep K in the inspiration phase (Middle tracing).

ducted with a more select group of patients in order, perhaps, to gain a more correct impression of the influence of pulmonary function on the ballistocardiogram

The following observations on the effect of position on the ballistocardiogram were made in the 31 cases studied

The amplitude of the systolic complex was diminished in the lateral positions, at times markedly so, with an occasional exception when the amplitude was of the same magnitude or better. J frequently became smaller in the lateral positions, and occasionally notched. H frequently became larger, L frequently became larger and occasionally notched. IJ was frequently shorter and variable in the lateral positions. K became deeper.

Occasionally an abnormal tracing appeared approaching normal when the patient was lying on the side of more extensive pulmonary involvement. But generally, when a tracing was abnormal in the prone position, it was also abnormal in the right and left lateral positions.

One abnormal tracing (class 3, Brown et al) in the prone position became normal in the right lateral position in the inspiratory and expiratory phases, but not in the resting phase. In one abnormal ballistocardiogram the right lateral resting tracing was normal, in another one it became normal in the right lateral position on inspiration only.

Of the 17 normal tracings in the prone position (in this group of 31

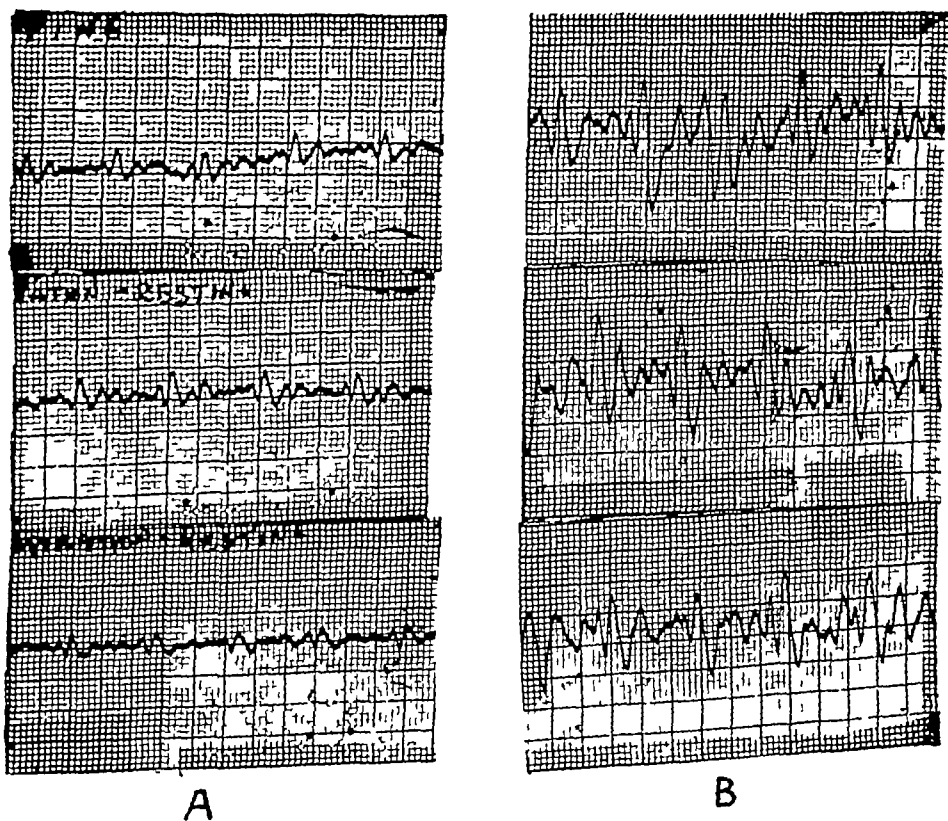


Figure 6A Tracing of a patient secured on June 2, 1953—Figure 6B Tracing of same patient on June 17, 1953. Note difference in amplitude. No demonstrable clinical or technical justification.



cases) only three tracings were normal in the lateral position—with variations, however, in the amplitude of the various systolic and diastolic components. Fourteen had abnormal ballistocardiograms (Brown—2 and 3) in the lateral positions. Since the abnormalities noted in this group were not only of amplitude but also of form and component relationship, the technical arrangement of the generating components cannot be held accountable. The fault must lie in the circulatory forces and their vectorial arrangement (Figs 10 and 11)

### Discussion

The statistical part of this report, is probably not of much significance. The figures would likely differ considerably in the next consecutive 100 cases. Only considerations of a general nature are permissible. In our earliest experience with the ballistocardiogram at Sea-View Hospital it became rather obvious that the graph is not a diagnostic expression of circulatory disease proper. On the contrary we were tempted to assume that the ballistocardiogram is more a reflection of "pulmonary physiologic

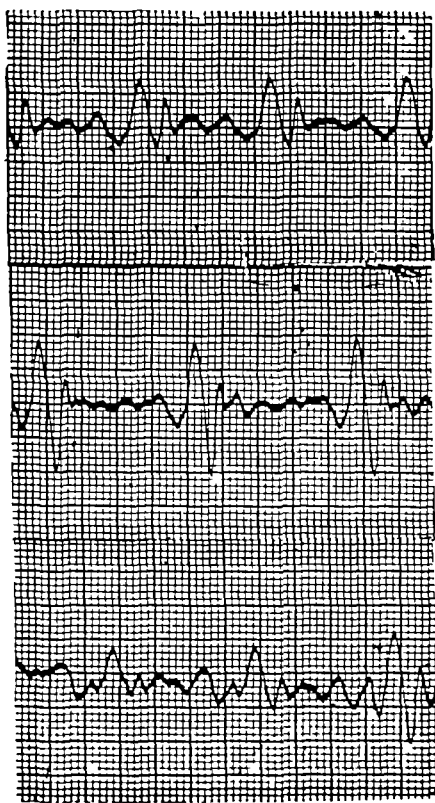


FIGURE 7

Figure 7 Upper tracing—normal respiration. Middle tracing—inspiration phase. Note deep K (paradoxical). Lower tracing—expiration phase. Most definite and stable Deep I (paradoxical).

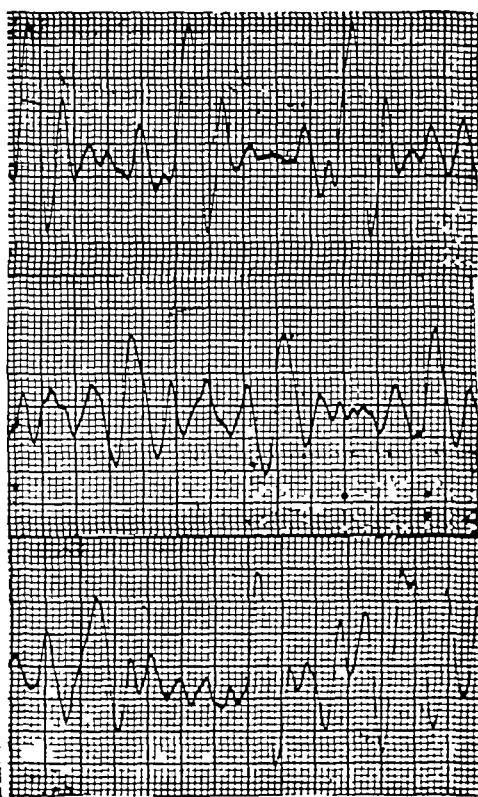


FIGURE 8

Figure 8 Upper tracing—normal respiration. Middle tracing—inspiration phase. Lower tracing—expiration phase. Compare I in inspiration and expiration. Note notching of H (?) in inspiration and L (?) in expiration.



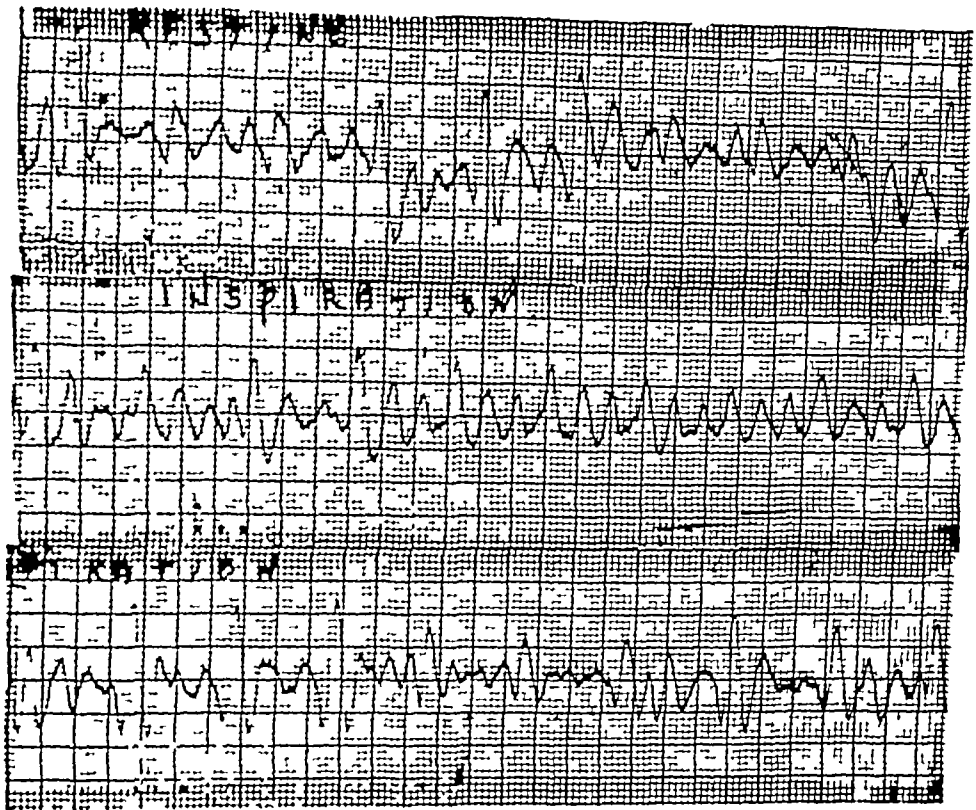


FIGURE 9. Case of herniation of right lung into left. Expiration tracing most definite and stable. I deeper than in the inspiration phase

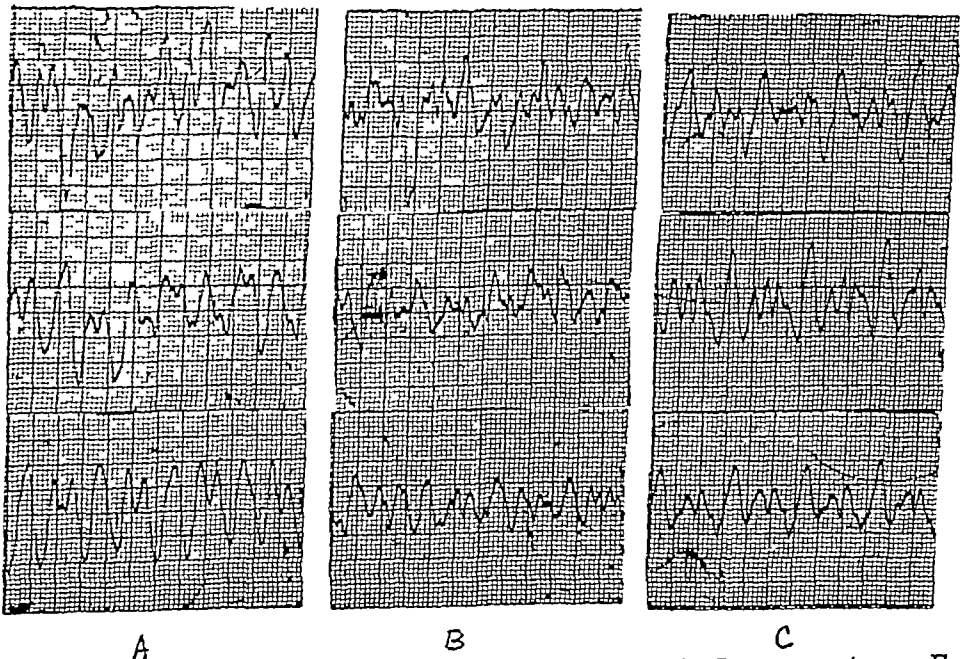


FIGURE 10. Case one of left pneumothorax. Figure 10A Prone position—Figure 10B Left lateral position—Figure 10C Right lateral position. Upper tracing—normal respiration. Middle tracing—inspiration phase. Lower tracing—expiration. Best tracing obtained in the right lateral position. The inspiration tracing is the most definable and normal.

state" rather than of cardiac or vascular abnormality. That the ballistocardiogram is dependent on respiratory function is a known fact.<sup>3</sup> It appears, however, that in the presence of pulmonary disease, this respiratory component is of major importance.

Is it because of the distorted pulmono-vascular anatomy or changes in the intrathoracic pressure due to respiratory arrhythmia that the aortic filling and the ventricular ejection become so chaotic so as to cause the marked structural changes in the tracing? Or are there other factors not readily explainable? Does the labile ballistocardiogram indicate an ever changing systemic circulatory state when pulmonary disease is present? Or does it represent variations in direction, quantity and force of the pulmonary circulation? To be more specific, is the short HI segment frequently observed in the inspiration tracing of our series due to para-

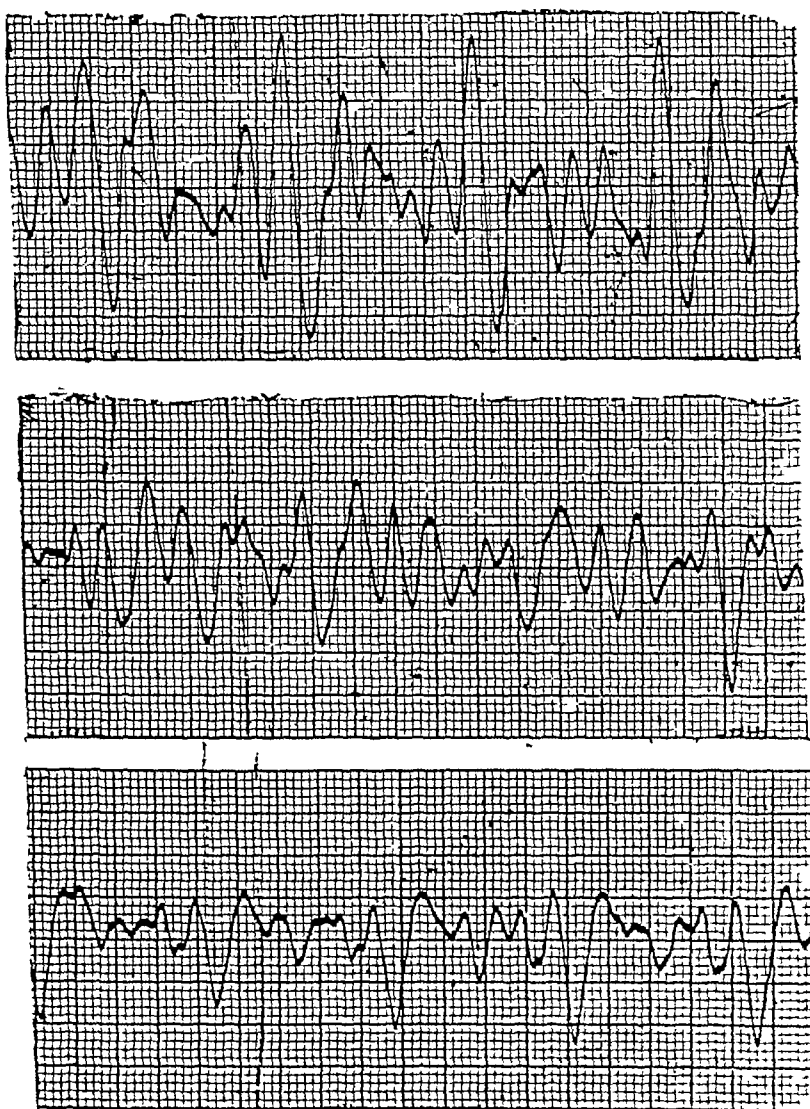


FIGURE 11 Upper tracing—inspiration phase in the prone position. Middle tracing—inspiration phase in the left lateral position. Lower tracing—inspiration phase in the right lateral position. Note IJ and JK relationship in the various positions as well as the variations in the form and amplitude of the diastolic waves.

doxical changes in the intrathoracic pressure—because of pleuro-pulmonary or pleuro-diaphragmatic adhesions? Or are there other factors not quite discernible at present to explain this phenomenon or the deep K when not expected or the exaggerated diastolic complexes? We have not observed in this analysis any constancy of sufficient degree in any of the components of the ballistocardiogram to permit cause and effect speculations. Only a few facts stand out prominently. Abnormal ballistocardiograms occur in patients with pulmonary disease in the absence of heart disease in all age groups. Age, however, seems to be a factor, in that the frequency of abnormalities increases with years. While in the general literature on the subject, one speaks of a ballistocardiogram below the age of 50 and above the age of 50, in patients with pulmonary disease the age of 40 seems to be a more distinct dividing line. Another observation of significance seems to be the fact that a single tracing obtained in the "usual" prone position may *perhaps* be sufficient in the patient without pulmonary disease, in the presence of pulmonary disease a tracing should not be considered abnormal unless obtained in various positions and various phases of respiration, and repeated in the same manner on the same or following day. Because of the extreme lability of the structure of the complexes in the presence of pulmonary disease a more liberal approach to the interpretation of the amplitude and form of the individual complexes is essential.

In a general way the following remarks are perhaps justified. Abnormalities observed under certain circumstances of stress are not dissimilar to the ones we observed in our series.<sup>4</sup> This suggests the possibility that changes induced by stress are at least in some measure dependent on the integrity of the respiratory mechanism. As an alternative, one would have to suspect that many changes in the ballistocardiogram are non-predictable, non-specific and not diagnostic of distinct cardiac or vascular entities and do not reflect *in all instances* the force of ventricular ejection. "The varying amplitudes of deflections obtained with repetitive recordings at the same amplification sensitivity also indicate that"—with the device employed in our study, the tracing cannot "be used to quantitate initial cardiac force in a manner similar to the method used with a ballistocardiographic table."<sup>5</sup> We have not observed any of the components of the ballistocardiogram to be the least variable and therefore more or less dependable for calculation purposes.

The role of extracardiac factors in producing ballistocardiographic abnormalities and particularly the role the pulmonary mechanism plays in altering some of the components of the ballistocardiographic tracing has been emphasized by other observers.<sup>6, 7, 8, 9, 10, 11, 12</sup> Thus, even in the presence of heart disease the H and L waves in the ballistocardiogram of mitral stenosis are stated to be due to changes in the pulmonary circulation. Our report further stresses the fact that abnormalities in the I wave, shortening of I-J stroke with increase in the prominence of the K wave, low amplitude and even generally indefinable patterns can occur in the absence of heart disease.

The importance of the pulmonary functional integrity in the structure of the ballistocardiogram is further attested by the fact that in certain cases the application of an abdominal binder may improve the appearance of the tracing<sup>13</sup> Such improvement in the ballistocardiographic picture is surely due to the improvement of the respiratory function by the elevated diaphragm as observed clinically by the application of an abdominal binder or the institution of pneumoperitoneum

Our study permits no speculation on the subject of genesis of the individual waves in the ballistocardiogram There is perhaps an indication, however, that both the H and L waves are related to the pulmonary status of the patient Following pneumothorax the amplitude of the H and L waves were diminished It would seem that the patho-physiologic state present in the diseased lung or in cases of pulmonary hypertension or in cases of cardiac failure is in some manner responsible for the increased amplitude of the H and L waves in certain cases

#### SUMMARY AND CONCLUSION

The ballistocardiograms of 100 consecutive cases of pulmonary tuberculosis in the absence of heart disease, were analyzed as to form and amplitude The number of abnormal tracings in all age groups was higher than that observed in the general population The abnormalities observed occurred in both the systolic and diastolic complexes of the tracing Some of the abnormalities were paradoxical, simulating reflection of circulatory stress rather than expressing respiratory dependence

It is suggested that in the presence of pulmonary disease, ballistocardiographic tracings should be secured in various positions and various respiratory phases, and that generally the interpretation of ballistocardiogram be more cautious and lenient

Grateful acknowledgement is made to Miss Katherine Moore and Miss Leonora Fox for rendering technical assistance in the preparation of this paper

#### RESUMEN

El balistocardiograma en 100 casos consecutivos de tuberculosis pulmonar en ausencia de afección cardíaca, se analizó en su forma y amplitud El número de trazos anormales en todas las edades fué más alto que el observado en la población general

Las anomalías observadas ocurrieron tanto en el complejo sistólico como en el diastólico de l trazo Algunas de las anomalías fueron paradójicas, simulando reflexión del esfuerzo circulatorio más bien que dependencia respiratoria

Se sugiere que en presencia de tuberculosis pulmonar, deben obtenerse trazos balistocardiográficos en varias posiciones y en diversas fases respiratorias y que generalmente la interpretación de los balistocardiogramas ha de ser cauta y no severa

#### RESUME

Les auteurs ont analysé dans leur forme et dans leur amplitude les balistocardiogrammes de cent cas de tuberculose pulmonaire chez lesquels

il n'y avait pas d'affection cardiaque associée. Le nombre des tracés normaux dans les groupes de tous âges fut plus élevé que celui qu'on observe généralement dans l'ensemble des individus non tuberculeux. Les anomalies qui furent notées atteignaient à la fois les complexes systoliques et diastoliques. Certaines d'entre elles donnaient paradoxalement l'impression d'une atteinte circulatoire beaucoup plus qu'une altération secondaire à une atteinte des voies respiratoires.

Les auteurs sont d'avis qu'au cours d'une affection pulmonaire, les tracés ballistocardiographiques doivent être pris en diverses positions et au cours de différentes phases respiratoires. Ils admettent que d'une façon générale, l'interprétation d'un ballistocardiogramme doit être prudente et réservée.

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# Surgical Trends in Pulmonary Tuberculosis\*

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There has been a tremendous change, during the past few years, in the manner in which we treat patients with pulmonary tuberculosis. If my former chief, Dr Ralph C Matson, were to attend one of our staff conferences at the University of Oregon State Tuberculosis Hospital today, I am sure that he would be greatly shocked to hear the recommendations that were being made. I, too, am sometimes disconcerted when I realize that for the vast majority of cases, presented at our conferences, we are ultimately recommending pulmonary resections. Those of us who had sanatorium experience in the 30's, or earlier, must be particularly aware that many of the patients whom we now subject to excisional therapy would have been considered then to have a good prognosis with nothing more than a prolonged period of bed rest. Furthermore, it is difficult to forget the trials experienced during the years when we were first exploring the values of pulmonary resection in the treatment of pulmonary tuberculosis.

The changes that have occurred in the surgical treatment of pulmonary tuberculosis, as they have evolved with us at the University Hospital, are evidenced by Table I which shows the numbers of certain operations that we have performed at four-year intervals since the hospital was opened late in 1939.

The thoracoplasty figures do not include "tailoring" thoracoplasties performed at the time of resections or decortications. They do include stages that were performed as separate operations before or after resections. The figure for the number of patients operated on is really that for the number of lungs subjected to major surgery. During the last two years an increasing number of patients have had bilateral surgery.<sup>1</sup> Figures for decortication or decortication with thoracoplasty are not included except in the totals.

TABLE I  
OPERATIONS PERFORMED AT THE UNIVERSITY STATE  
TUBERCULOSIS HOSPITAL  
*Portland, Oregon*

	1940	1944	1948	1952
Pulmonary resections	0	16	19	85
Thoracoplasties (all stages)	20	57	106	13
Extrapleurals	29	1	1	3
Other major operations	0	0	6	2
Total Major Operations	49	74	132	113
Total Minor Operations	87	48	45	7
First-stage thoracoplasties	11	20	41	8
Number patients having major operations	40	37	67	100

\*Presented at the First Annual Session of the Western Tuberculosis Conference, Salt Lake City, Utah, Sept 18, 1953

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Figure 1 illustrates graphically how our use of various operative procedures has changed each year since 1940 at the University Hospital. It should be noted that the surgical program in this hospital, which has only 80 beds, has always been active. The hospital admissions are generally selected from patients who are likely to be candidates for surgery and patients who, because of complications, may require the special facilities provided by the medical school. In 1940, when most of our patients received artificial pneumothorax therapy, most of the operative procedures were classified as minor and included primarily closed intrapleural pneumonolyses and phrenic nerve interruptions. Of the major operations performed in 1940, extrapleural collapse procedures predominated. Dr. Matson's extrapleural pack (gauze packing, sometimes impregnated with oil of gomenol or iodoform, encased in a sheet of plastic flexi-tissue) was giving most encouraging early results. Late complications in patients so treated—infections and fistulae—caused us to return to thoracoplasty for more and more of the patients in whom surgical collapse seemed indicated. The use of thoracoplasty reached its peak in 1948. The sharp increase in the number of thoracoplasties during that year reflected the shorter period of preparation for surgery required when patients were given streptomycin and the increased safety and improved results of surgery in patients so treated.

The number of first stage thoracoplasties performed each year approximates the number of patients on whom thoracoplasty was performed as a primary procedure. While during most years there was an average of almost three stages performed on patients undergoing thoracoplasty, the average has now dropped to less than two. During the last four years the number of primary thoracoplasties has dropped in inverse ratio to the increase in the number of resections performed. In fact four of the eight first stages performed during 1952 were post-resection thoraco-

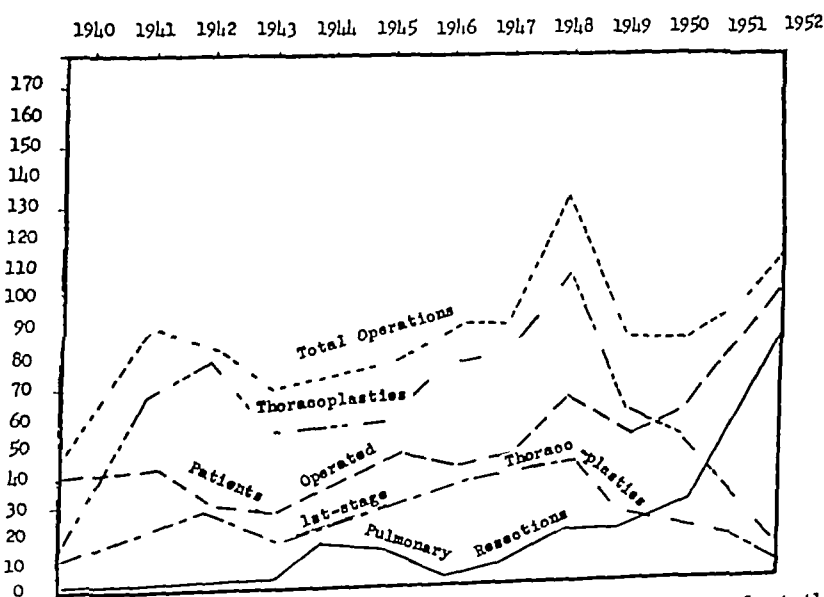


FIGURE 1 Graphic illustration of various operative procedures used at the University State Tuberculosis Hospital, by years (see text)

plasties    Of the four primary thoracoplasties, two were performed in one stage, one in two stages and one in three

Insofar as pulmonary resections are concerned it will be noted that we did a number in 1944 and 1945    There were enough serious complications in this group of resections to cause a marked decrease in the number of resections undertaken during the next two years    Resections were again undertaken in larger numbers following the advent of streptomycin and the results have seemed so gratifying that, as the graph indicates, we are now performing them almost to the exclusion of all other types of surgery for tuberculosis    The serious complications of resection have become much less frequent and are more readily controlled since the antimicrobial drugs for tuberculosis have become available    But the mere fact that resection for pulmonary tuberculosis is safer now than formerly is not in itself a valid reason for preferring resection to collapse therapy    I propose therefore to explore the reasons for which we, and many others who treat tuberculosis, have largely abandoned the use of the older, well tried forms of collapse therapy in favor of resection therapy

#### *Artificial Pneumothorax and Closed Intrapleural Pneumonolysis*

Ten years ago few experienced phthisiologists would have questioned the statement that artificial pneumothorax was the treatment of choice in most cases of pulmonary tuberculosis in which there were no contraindications and in which an adequate collapse could be established    In some cases it was considered the *sine qua non* for possible arrestment of the disease    At our staff conferences, in discussing the management of new admissions, first consideration was generally given to the advisability of trying artificial pneumothorax    In perhaps 80 per cent of patients an attempt to establish it was made, either as soon as preliminary studies had been completed or after a period of bed rest had shown little or no improvement    Not only could it control some far advanced lesions which tended to progress on a strict sanatorium rest regime, but there was also considerable evidence that patients with small cavities, or even those with minimal exudative disease, were less likely to manifest late reactivation if subjected to two or more years of pneumothorax collapse

We are all aware that artificial pneumothorax, with the aid of pneumonolysis where indicated, has arrested the disease or prolonged the lives of hundreds of thousands of patients with pulmonary tuberculosis    It still can do so    It could do so better now than formerly, since antimicrobial drugs are eminently effective in overcoming most of the contraindications to and the complications of artificial pneumothorax therapy

But it remains to be seen whether artificial pneumothorax will have any place at all in the future treatment of pulmonary tuberculosis    Because of economic considerations involved in a type of treatment which is relatively prolonged and inconvenient for the patient, because of late complications (such as tuberculous empyema, bronchopleural fistula and non-expandable lung) and because of an appreciable incidence of late reactivations occurring in patients treated thus in the past (for the most



FIG  
2AFIG  
2BFIG  
2CFIG  
2D

V L White male, age 42 Minimal pulmonary tuberculosis diagnosed in 1940 Sanatorium care in 1940 for three months, in 1942 for six months and in 1945 (*Figure 2A*) for 14 months In 1945 left artificial pneumothorax was established

First admitted to University State Tuberculosis Hospital in 1947 when right pneumothorax and pneumonolysis were performed Readmitted to University State Tuberculosis Hospital in 1952 (*Figure 2B*) when the apical and posterior segments of the right upper lobe were resected and the remainder of the right lung was decorticated The patient had severe essential hypertension (BP 220/140) and so right sympathectomy (T2 to L2) was performed at the same time

During decortication the right phrenic nerve was inadvertently severed It was resutured, however postoperative diaphragmatic paralysis was considered largely responsible for the very stormy postoperative course The patient was unable to raise his secretions and developed atelectasis, (*Figure 2C*) despite repeated tracheobronchial aspirations A persistent air leak required a secondary thoracotomy about two weeks later

Because of the stormy course this patient refused the contralateral surgery which had been contemplated He reconsidered, however, and returned a year later for decortication on the left with wedge resections of large granulomas in both the upper and the lower lobe A left dorsal sympathectomy (T2 to L1) was performed at the same time Convalescence from this operation was smooth (*Figure 2D*)

This patient's last positive sputum was just before his last operation in April, 1953 He was discharged from the hospital in July, 1953 In October 1953 his condition seemed excellent He was moderately active His blood pressure had stabilized at about 130-140/100 and his right hemidiaphragm had a normal excursion of about 4 cms indicating phrenic nerve regeneration

- (A) Prior to establishment of left artificial pneumothorax
- (B) Prior to right decortication, resection and sympathectomy, when right phrenic nerve was inadvertently severed.
- (C) Postoperative atelectasis and persistent "air leak," requiring secondary thoracotomy
- (D) Following left decortication, resection and sympathectomy

part before the advent of streptomycin), we have practically abandoned the use of artificial pneumothorax. I suspect that Dr. Matson, and other pioneers, would be greatly disheartened by the feeling that their extensive clinical research had been cast overboard. We would wish them to know that this work has not been wasted. After all, the good it has already accomplished in the salvage of human life is of inestimable magnitude. But we further owe it to these early workers, as well as to our patients, to determine whether or not indications for artificial pneumothorax in pulmonary tuberculosis may still exist. I shall be particularly interested to know what becomes of patients who are treated with artificial pneumothorax, perhaps only for relatively short periods, in conjunction with long continued antimicrobial therapy. Undoubtedly there are investigators who will determine this. We still feel that short-term artificial pneumothorax, along with medical treatment, may have value in promoting stabilization of active disease preparatory to contemplated lung resection, even if it does not eliminate the need for such a resection.

### *Phrenic Nerve Interruption*

While interruption of a phrenic nerve has certainly had its place in phthisiotherapy, I am convinced that it not only has been used too frequently in the past but that its indications will become increasingly restricted in the future. Never particularly dependable for the "collapse" treatment of parenchymal lesions, it has always carried with it the possibility of undesirable sequelae and complications.

Permanent paralysis of a hemidiaphragm results in rather severe permanent loss of respiratory reserve. While phrenic interruption by crushing, the only acceptable procedure today, is usually followed by regeneration and return of function, complete return of function is probably seldom achieved and permanent total loss of function occurs at times. As measures for treating pulmonary tuberculosis which involve minimal loss of respiratory reserve become more generally available, preservation of function assumes an increasingly important place in the management of this disease.

In treating pulmonary tuberculosis it is also important to keep in mind that failure to control the disease, or its later reactivation, may require the use of surgical therapy which was not at first contemplated. It is well established that patients who have a paralyzed hemidiaphragm are more difficult to manage properly and more prone to develop complications following any major surgery that may become necessary. Figure 2 (Case VL) illustrates such a case.

During the past year we have performed phrenicomyotomy twice in patients who had persistent "air leaks" following pulmonary resections. In both it appears to have been helpful. We do not recognize any other indication for this procedure at present, though others still often employ it (usually combined with pneumoperitoneum) in patients who are not considered to be candidates for resection or thoracoplasty.

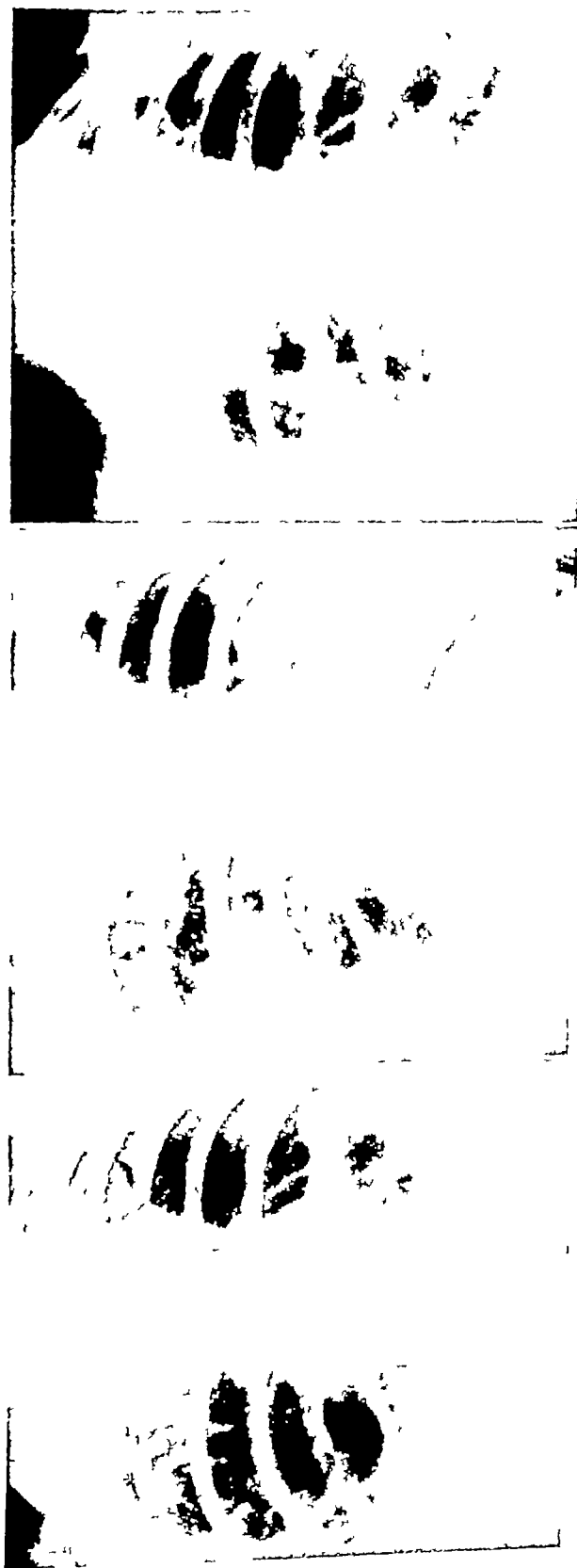


FIGURE 3A

FIGURE 3B

FIGURE 3C

M M a white female, age 49. Pulmonary tuberculosis first diagnosed in 1934 following pregnancy. Treated with bed rest, left pneumothorax (22 months), sandbags and gold salts. In 1936 a new lesion developed on the right side at the time of another pregnancy. Treatment included bed rest and light phrenephriaus. Apparently well until 1951 when she was admitted, following an acute febrile illness, with far-advanced bilateral pulmonary tuberculosis (Figure 3A). Gratifying response to antimicrobial drugs and pneumoperitoneum (Figure 3B). Thoracoplasty performed preliminary to contemplated resection. Resection later considered unnecessary (Figure 3C). Has been home and fairly active since September, 1952. Last positive sputum was in October, 1951.\*

\*A small cavity has recently opened beneath this thoracoplasty. Pulmonary resection may still become necessary.

*Pneumoperitoneum*

We find that our use of artificial pneumoperitoneum has increased as our use of artificial pneumothorax has fallen off. Particularly in conjunction with antimicrobial therapy and bed rest, pneumoperitoneum apparently tends to promote healing of tuberculous disease, but its use in a large proportion of sanatorium patients, as recommended by some, still is controversial. Usually we do not consider that this combination effects sufficient resolution to obviate the need for more definitive surgery. It is a combination that has seemed useful in patients whose disease is of such a nature or extent that other types of active therapy are too hazardous, or otherwise contraindicated. More often it is a therapeutic regime which we may use for several months to prepare patients for unilateral or bilateral resections. Despite hopes to the contrary, the resections have eventually almost always seemed necessary.

A house doctor on our service once had the grave misfortune of producing fatal air embolization while giving a pneumoperitoneum refill. Such a disaster, rare though it be, emphasizes the fact that what seems an innocuous procedure is not without some danger and that there should be ample justification before it is used.

*Thoracoplasty*

There was a time when we would recommend thoracoplasty for practically all cases of cavitary disease, particularly unilateral, in which adequate artificial pneumothorax could not be established. We perform few primary thoracoplasties today. They are done occasionally for cavitary disease which is predominantly in the upper lung field, when there is such extensive scattered involvement in the remainder of the lung that subtotal lung resection appears to be out of the question. Very sick patients for whom resection appears necessary can often be improved by thoracoplasty, along with antimicrobial therapy, to the point where lung resection can be performed with much greater safety. In a couple of cases, treated in this way, the contemplated resection was later considered unnecessary (Fig 3). More often, however, primary thoracoplasties which were expected to control the disease have failed to do so and lung resection has eventually had to be performed.

At present we seldom perform thoracoplasty except as an adjunct to resection. We feel that the standard thoracoplasty, devised by Alexander for adequate collapse of upper lung disease, involves excessive loss of function due to the necessity of collapsing good as well as diseased lung, due to the scoliosis which is frequently unavoidable, and due to considerable trauma to the muscles and nerves of the chest wall and shoulder girdle. If all the significant disease can be resected without performing thoracoplasty, or with only a concomitant "tailoring" thoracoplasty such as we have described in a previous publication,<sup>2</sup> there is good evidence, both subjective and objective,<sup>3</sup> that much more respiratory function can be preserved.

While evidence appears to be accumulating to discount the wide-spread belief that over-distention of remaining lung tissue, following pulmonary resection, contributes significantly to loss of pulmonary function or promotes exacerbation of non-resected tuberculous lesions<sup>3, 4</sup> we still consider it advisable to obliterate, at least partially, any large dead space remaining following resection. A "tailoring" thoracoplasty involves practically no deformity and, properly performed, it doesn't collapse non-involved lung tissue. It prevents excessive distortion of trachea, bronchi and pulmonary vessels and aids in the prevention or control of the complications which sometimes occur following resection. We have been performing thoracoplasties at the time of resection in about 25 per cent of those resected. When thoracoplasty is performed in advance of resection the same type of thoracoplasty should be performed—i.e., anterior segments of ribs below the first should be preserved, as should the transverse processes. However, we recommend that posterior rib stumps not be left as long as may be feasible in a concomitant "tailoring" thoracoplasty, so as to increase the possibility that later resection may be avoided. Occasionally thoracoplasty is performed two or three weeks following resection as when the remainder of the lung fails to fill the space as anticipated, when there is persistent air leak from the raw surface of the partially resected lung, or rarely, when the additional surgery is considered inadvisable at the time of resection. When thoracoplasty is delayed, proper "tailoring" cannot be effected as well. We therefore prefer the concomitant or preliminary thoracoplasty, though others do thoracoplasty subsequent to an upper lung resection or pneumonectomy almost routinely.

### *Other Surgical Collapse Procedures*

It is possible that modifications of the standard thoracoplasty, including Overholt's costo-inversion thoracoplasty and extraperiosteal plombage followed by thoracoplasty, and the various types of extrapleural pneumothorax and plombage may continue to have a place in phthisiotherapy. These procedures deserve special consideration for patients with widespread bilateral disease when respiratory reserve is at a critical level, and particularly when there is considerable question as to a patient's ability to tolerate the thoracotomy necessary for a possible resection—e.g., following contralateral pneumonectomy. We feel that extrapleural pneumothorax and plombage can be performed with much greater safety now than before antimicrobial drugs were available, and yet, when such procedures are considered, we generally decide that resection is just as safe and offers a much more definitive approach and a much better long-term prognosis.

### *Decortication*

In patients who have had pulmonary tuberculosis, decortication is generally performed to achieve re-expansion of a lung which is non-expandable as a result of prolonged artificial pneumothorax. Presumably decortication will be required less often in the future as the use of artificial

pneumothorax becomes less prevalent and particularly as antimicrobial drugs reduce the incidence of pleural complications, with or without pneumothorax being present. In about 50 per cent of patients on whom we have performed decortications following prolonged pneumothorax therapy, which presumably has arrested the disease, we have found and removed caseous foci in the underlying lung. Such foci are considered a potential source of late exacerbations and probably account for late development of contralateral spreads, such as are seen all too frequently in patients who are receiving, or have received, pneumothorax therapy. Significant parenchymal lesions found at the time of decortication should be removed, often by wedge or segmental resection (Fig 2). Whether or not resection has been performed, the long collapsed lung sometimes will not expand adequately to fill the hemithorax following decortication. Under such circumstances we usually perform concomitant thoracoplasty for the same reasons that we do so with resections.

Decortication of non-expandable lungs, often combined with partial resection, should help to prevent late complications, such as empyema, fistulae, exacerbations and spreads. It is now recommended at an earlier time after the appearance of a thick "peel" than has generally been accepted in the past. While it is frequently amazing how much volume and function can be recovered in a lung that has been collapsed for many years, it is undoubtedly true that the longer the collapse has existed the less recovery can be anticipated.

In tuberculous and mixed infection empyema, with or without bronchopleural fistula, decortication will probably always find its indications. In many cases enzymatic debridement and antimicrobial therapy should first be given adequate trial. Enzymes must be used with caution, however, if at all, in the presence of a bronchopleural fistula. Jones et al.<sup>5</sup> reported acute disseminated tuberculosis developing in three out of eight cases treated with enzymes, presumably because the thinned infected fluid was more readily aspirated through fistulae. Having had one such experience, we have avoided risking repetition.

An application of decortication which I have not seen mentioned in the literature is that for patients with organized pleural exudate where the diagnosis has not been established by the usual laboratory means. In one such patient the clinical picture strongly suggested malignancy with pleural invasion, and in another the referring doctor's diagnosis was Friedlander's empyema. Both were found to have tuberculous empyema at the time of decortication, and both were much improved by surgery. Decortication may well be recommended for diagnosis as well as treatment when the cause of persistent pleural exudate remains obscure.

### *Cavity Drainage*

It is a long time since we have encountered a case in which Monaldi cavity suction drainage or cavernostomy seemed indicated. The mechanisms which produce "tension" cavities are generally eliminated by antimicrobial therapy. Even if they are not, resection again appears to be

the more definitive approach and is better performed before one has established an infected fistulous tract through the chest wall. Under unusual circumstances, however, the indications for such procedures may occasionally be encountered, particularly in far-advanced cases for whom resection seems too hazardous, or in order better to prepare a sick patient for a contemplated resection. The potential value of such procedures should therefore be kept in mind.

### *Pulmonary Resection*

As is evident from what has been said above, pulmonary resection has appeared to be indicated in an increasingly large percentage of the patients under our care. Discussions at our conferences now seem most frequently to be concerned with the possible need for pulmonary resection, and the most opportune time for its performance when it appears indicated.

Today, as formerly, we consider that there are certain obligatory indications for resection. The presence of large "solid" lesions ("tuberculomas"), suspected neoplasm, destroyed lobes and lungs, cicatricial bronchial stenosis with significant bronchopulmonary disease distal to the stenosis, significant tuberculous bronchiectasis demonstrated by bronchography or tomography, and lesions which continue to be the source of positive sputum despite collapse and antimicrobial therapy are among the indications which we still consider incontrovertible. In most of the patients with such indications, we feel that resection should not be too long delayed. If there are acute exudative lesions present, we attempt to achieve maximum resolution and stabilization of such lesions by medical therapy, often with the aid of pneumoperitoneum, before resection is



FIGURE 4A

FIGURE 4B

H. T. Chinese male, age 23. Pulmonary tuberculosis diagnosed March, 1952. Admitted July 16, 1952 with rapidly progressive disease (Figure 4A). Excellent response to antimicrobial drugs with bed rest and pneumoperitoneum (Figure 4B). Repeated body section radiograms failed to reveal any residual evidence of cavitation or of granulomatous lesions. Sputum has been continuously negative since February, 1953. On admission this patient was considered a possible candidate for bilateral resection.

undertaken. This may require six months or more. Otherwise, resection is sometimes performed after only six weeks or less of preliminary study and antimicrobial therapy. Prompt resection of a solitary lesion is mandatory if one suspects that it may prove to be a malignant neoplasm.

"Tension" cavities no longer constitute an indication for early resection, in our opinion. Remarkable results are sometimes seen following prolonged medical therapy (Fig 4), but most patients who have had a "tension" cavity do come to resection. When continuing improvement is no longer demonstrable roentgenographically, we feel that these patients should be thoroughly studied, particularly with body section radiograms, with bronchoscopy and sometimes with bronchography, in order to determine whether there are residual lesions for which resection may be advisable.

The great increase in the number of resections which we perform has resulted largely from acceptance of the concept of Medlar et al.<sup>6,7,8</sup> that certain tuberculous lesions, often quite small, may persist as necrotic foci containing viable tubercle bacilli though treated adequately by past standards, and that these foci present a considerable hazard as a potential source of later spread or exacerbation. When well-defined tuberculous nodules, which are not calcified, are demonstrated by body section radiography and when they persist following prolonged medical therapy, we seriously consider the advisability of resection, especially if one or more of these exceeds 1 cm in diameter and particularly if sputum cultures have been positive. Fibrotic contracted segments or lobes are also considered indications for resection. We are no longer satisfied with converting the sputum to negative in many of these cases. We are inclined, rather, to resect lesions which may persist as potential sources of new disease.

We are aware that many of the lesions which we have resected might have healed, and never reactivated, had the patients been subjected to prolonged medical management and appropriate precautions following discharge from a sanatorium. Mitchell, however, has reported at least one known progression of the disease in 35.8 per cent of 589 patients with minimal pulmonary tuberculosis who were treated with modified bed rest at Trudeau Sanatorium.<sup>9</sup> Admittedly we are sometimes influenced in our recommendations by the shortage of sanatorium beds in our area and by the resultant need to maintain a relatively rapid turnover in the patients who are institutionalized. We are aware, too, that many patients with lesions such as we now resect have in the past had their tuberculous disease satisfactorily controlled by collapse therapy, carried out for long periods or for the remainder of their lives. But we know that, in the past, a significant percentage of patients treated by such methods have had to be readmitted because of reactivation of their disease and we believe that, with resection, this percentage can be materially reduced or practically eliminated. We do not yet know, unfortunately, whether the percentage can be reduced to a comparable degree as a result of adding antimicrobial therapy, without resection, to other types of



treatment in such cases. Evidence may accumulate within the next few years which will support those who feel that the pendulum has already swung too far toward a radically high proportion of resections in tuberculosis. Discovery of new and more efficient antimicrobial drugs and combinations of drugs may also alter the indications for resection. On the other hand, emergence and persistence of drug-resistant strains of tubercle bacilli in some of these patients may assume a role of increasing importance in the future and make it the more imperative to resect lesions while a patient's organisms are still sensitive to antimicrobial medications.

Pulmonary resection has become increasingly important in the management of cases of far-advanced bilateral pulmonary tuberculosis. As Woodruff has shown,<sup>3</sup> resection causes less physiologic alteration than thoracoplasty. When conservation of function reaches a critical level, because of the extent of the pathology, it is often possible to control the disease by multiple bilateral segmental and local excisions<sup>1</sup> when thoracoplasties or other types of collapse therapy would excessively reduce respiratory reserve because of the inevitable simultaneous collapse of healthy lung tissue.

The techniques of resection have become well enough standardized so that they do not require detailed discussion here. We still prefer to perform a "tailoring" thoracoplasty at the time of upper lung resections if there has been so much reduction in lung volume that a large dead space is left. While there is evidence that "over-distention" of the remaining portion of the lungs may be of little or no significance from the standpoints of function and reactivation,<sup>3, 4</sup> tracheobronchial distortion can produce annoying symptoms and even a small concomitant thoracoplasty appears to have definite value in the prevention of this and in the prevention and control of empyema and bronchopleural fistula. It also may have value in preventing the cardiocirculatory embarrassment which can result from excessive mediastinal displacement.

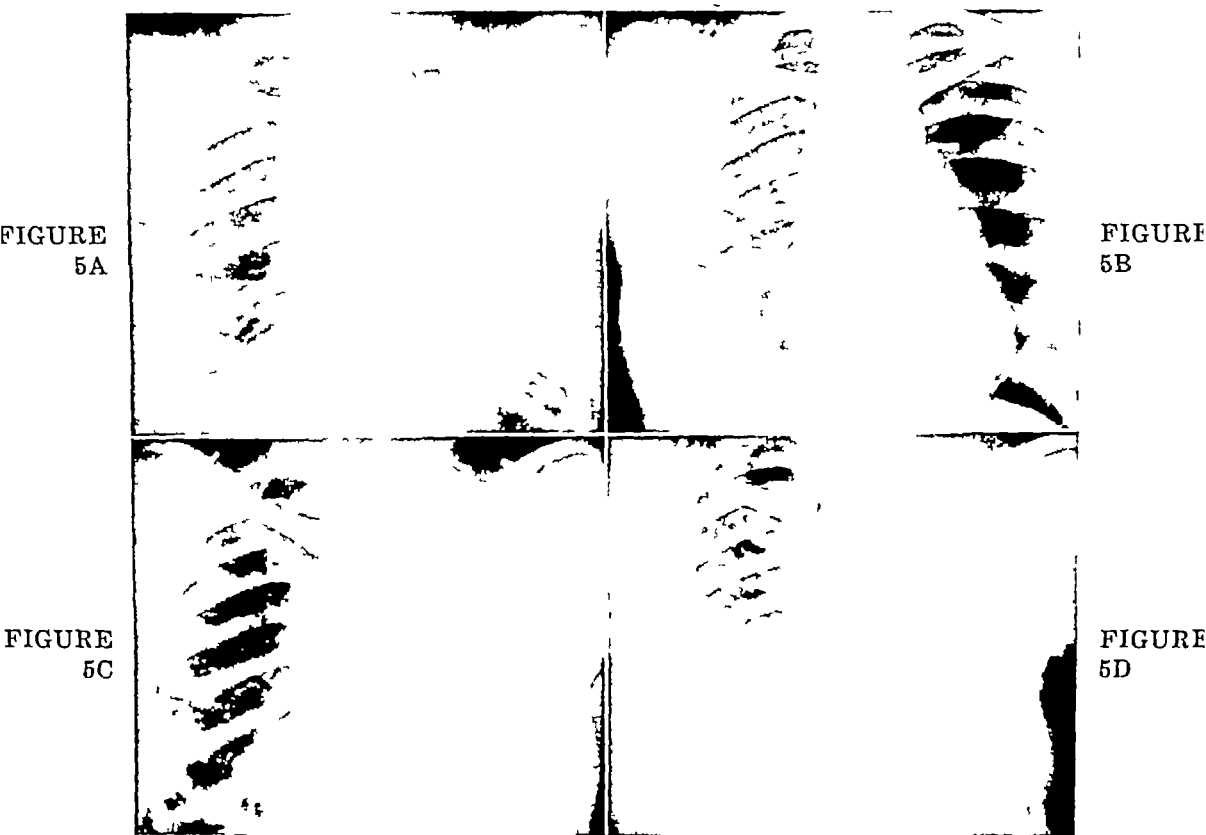
When bilateral resections are contemplated the more involved side is generally operated on first. We feel that simultaneous bilateral resections, such as have been performed by Overholt, and perhaps others, probably introduce additional unnecessary hazard in most instances. Furthermore, if the worse side is subjected to resection first, it is possible that, in some instances, the contemplated contralateral resection might later prove to be unnecessary. When decortication, with or without resection, seems indicated on one side we may prefer to perform this before resecting the more serious disease in the contralateral.<sup>1</sup> We feel that we may thus be able to improve respiratory function sufficiently to make the contralateral resection less hazardous. When both sides are to be operated on we generally allow a period of three or more months of convalescence between the two operations.

Widely distributed major tuberculous lesions in one or both lungs can sometimes be resected by enucleations, wedge and segmental resections, with maximum conservation of function. The good results which we have

had with bilateral as well as unilateral resections for tuberculosis, the decreased number of procedures involved as compared with thoracoplasty and extrapleural collapse, the decreased length of hospitalization and decreased morbidity, all incline us towards resection rather than collapse surgery whenever it seems likely that all major tuberculous foci can be eradicated. We have never performed resection following a contralateral pneumonectomy but believe that situations are encountered where such should be considered (Fig 5)

### *Tracheobronchoplasty*

In discussing the surgery for pulmonary tuberculosis some mention should be made of the brilliant work of Gebauer<sup>10, 11</sup> and others who have performed plastic repairs of damaged and stenotic portions of the tracheobronchial tree. When we encounter bronchial stenosis, which seems to be



F S, w, f, age 34. Pulmonary tuberculosis diagnosed 1942 following pregnancy (Figure 5A). Left pneumothorax initiated with conversion of sputum in three months (Figure 5B). Sputum positive in 1943 and active tuberculous bronchitis diagnosed. Treated with topical silver nitrate and pneumothorax converted to oleothorax (Figure 5C). Sputum negative. Five-rib thoracoplasty in February, 1953, oil being aspirated. Pleuropneumonec-tomy with resection of three more ribs on March 17, 1953 (Figure 5D). Sputum has been negative since January, 1952.

The film of October 8, 1952 (C) shows a round lesion at the right base. We considered the possibility that this might be neoplastic, but it gradually diminished in size (D). Had it not decreased in size or had it become larger, this lesion would have been resected despite the contralateral pneumonectomy.

far more rare in our area than it used to be, we generally find extensive bronchopulmonary disease distal to the stenosis, making resection obligatory. We have, however, found bronchoplasty a valuable aid to conservation of healthy lung tissue in a few instances and its potentialities should not be neglected.

### *Postoperative Care*

It is proper, no doubt, to add here a few words regarding certain changes which have been evolving in our postoperative care of patients with pulmonary tuberculosis. Except in acutely ill toxic patients we no longer adhere to the very strict rest regimes which formerly were the rule. Following surgery we subscribe to a program of early ambulation, such as is now used in the postoperative care of most surgical patients, except that in the tuberculous patients it is instituted more gradually and over a considerably longer period of time. The average patient who has had resection is required to "dangle" and is permitted use of the bedside commode by the first or second postoperative day. He is allowed to go to the bathroom twice a day as soon as his strength permits. Barring complications or evidence of residual active disease, a graduated schedule of "up time" and walking exercise is begun approximately six weeks following surgery. Activities are gradually increased until, by the end of the third or fourth month, the patient is generally discharged from the hospital on a schedule which permits four hours sitting up in a chair and one hour of walking exercise. Many patients are permitted full activity, and even return to work, within six months following surgery, as long as there is no roentgenographic evidence of residual or new lesions for which a continued rest regime is considered mandatory.

The presence or absence of such lesions also determines the length of time that antimicrobial medications are prescribed. During the two-week period immediately following major surgery the dosage of streptomycin or dihydrostreptomycin, or combination of the two, is generally increased to 1.0 gm daily. Thereafter we return to a schedule of 1.0 gm twice a week, always giving PAS, 12.0 gm daily, or INH, 4-6 mg per kilogram daily, or both, throughout the period of streptomycin therapy. Antimicrobial therapy is sometimes discontinued when the patient is discharged from the hospital, provided no residual lesions are evident, though we have followed the tendency to give these medications for more prolonged periods. If there are residual lesions by x-ray film examination the drugs are always continued for varying periods following discharge, even though such lesions appear stable.

The types of thoracoplasty which we now perform, either alone or in conjunction with resection, rarely require postoperative measures to overcome paradoxical motion or to combat scoliosis, though one of my associates, Dr. Lawrence Lowell, has purposely performed extensive one-stage thoracoplasties on two or three occasions during the past year and has combated paradoxical motion by use of a plaster cast, as recommended by Trapp.<sup>12</sup>

Postoperative measures to prevent or relieve pulmonary atelectasis have not changed. They should be used regularly and conscientiously. The potential value of tracheostomy in patients with critically lowered respiratory reserve and those who fail adequately to eliminate bronchial secretions should always be kept in mind.

Following sub-total pulmonary resections we generally maintain water-seal drainage of the pleural cavity with one large intercostal drainage tube for an average period of 48 hours, the length of time being varied according to the amount of drainage and the persistence of air leaks. When air leaks are extensive at the conclusion of a resection, two drainage tubes may be used, as is also generally the case following decortications. In the absence of significant air leaks we occasionally close the chest wall without drainage. Drainage is not established following total pneumonectomy unless there has been empyema present. Under such circumstances we are likely to perform concomitant thoracoplasty, place a large intercostal tube posterolaterally for drainage and a small polyethylene tube anteriorly for introduction of irrigating solutions containing antibiotics or enzymes. Such a polyethylene tube has also proved of value in some cases of sub-total resection, to permit escape of air and for introduction of medications. When persistent air leakage prevents early obliteration of the pleural cavity constant strong suction may be all that is required. If this fails, consideration should be given to performing thoracoplasty, phrenic nerve crush or a second thoracotomy in order to suture any major leaks.

Following surgery we consider deep breathing and arm exercises important in order to recover maximum function.

#### DISCUSSION AND SUMMARY

Like others, we have practically abandoned the use of artificial pneumothorax, phrenemphraxis and primary thoracoplasty in the treatment of pulmonary tuberculosis. Most of the patients on our service who do not manifest adequate resolution of their disease under medical management, become candidates for pulmonary resection, unilateral or bilateral.

Pulmonary resection is preferred to collapse therapy because

- 1) It is considered to offer a more definitive and permanent means of control
- 2) It is generally more conserving of respiratory function
- 3) It avoids the late complications of artificial pneumothorax and extra-pleural plombage
- 4) It generally results in immediate sputum conversion
- 5) Patients, usually, have a much shorter period of morbidity and can be rehabilitated earlier
- 6) It permits a more rapid hospital turnover, reducing the bed shortage and permitting definitive treatment of a much larger number of patients during a specific period of time
- 7) We believe that its wider use will materially reduce the number of readmissions due to reactivation and spread of disease

- 8) Concomitantly there should be public health benefits if infectiousness is more readily and promptly controlled
- 9) By reducing the length of therapy required for treating the individual patient the economic savings, to the patient and the State, should become of great magnitude

I admit that we may be using resection therapy too widely. We may learn that the antimicrobial medications now available, and new ones which will doubtless be discovered, can obviate the need for much of the surgery which we now perform. I have tried to review the trends which the surgical treatment of pulmonary tuberculosis has shown in our hands and certainly in those of many others. We must, however, continually re-evaluate our position. I have not attempted to offer statistics concerning the results of treatment, feeling that they would not have much value, as yet, from the standpoints of numbers and of time. In another 10 years we may look back on this heyday of resection as we do now on that of pneumothorax therapy. For while time is said to heal all wounds, it must also wound all those who would continue to heal by the convictions of yesterday.

#### DISCUSION Y RESUMEN

Como otros hemos prácticamente abandonado el uso del neumotórax artificial, así como la toracoplastia primaria en tuberculosis pulmonar.

La mayoría de los enfermos de nuestro servicio que no demuestran adecuada resolución de la enfermedad bajo tratamiento médico, se convierten en candidatos a la resección pulmonar y sea un o bilateral.

La resección pulmonar se prefiere en lugar del colapso por

- 1) Que se considera que ofrece un medio más definitivo y permanente de control
- 2) Generalmente conserva más la función respiratoria
- 3) Evita las complicaciones tardías del neumotórax artificial y del plomaje extrapleural
- 4) Generalmente se logra la inmediata conversión de los esputos
- 5) Los enfermos tienen un período de morbilidad más corto y se pueden rehabilitar más pronto
- 6) Permite una renovación más rápida de enfermos en el hospital, disminuyendo así la escasez de camas y permitiendo tratamiento definitivo a mucho mayor número de enfermos en un determinado tiempo
- 7) Creemos que su uso más amplio reducirá materialmente el número de readmisiones debidas a la reactivación de la enfermedad
- 8) Al mismo tiempo habrá beneficios para la salubridad pública si la comunicabilidad es más prontamente controlada
- 9) Disminuyendo la duración del tratamiento requerido para el enfermo individual la economía tanto para el enfermo como para el gobierno debe ser muy considerable

Admito que podríamos estar usando la resección demasiado ampliamente.

Podríamos aprender que la medicación antimicrobiana hoy obtenible y la que sin duda habrá de descubrirse, pueden evitar el uso de mucha de-

la cirugía que ahora realizamos. He tratado de revisar las tendencias que el tratamiento de la tuberculosis ha mostrado en nuestras manos y por supuesto en las otras. Sin embargo, debemos reevaluar constantemente nuestra situación. No intento ofrecer estadísticas del resultado del tratamiento, porque creemos que no habrán de tener gran valor tanto por su número como por el tiempo. Dentro de otros 10 años veremos retrospectivamente hacia este entusiasmo por la resección como vemos ahora el que se tenía por el neumotórax. Porque si bien se dice que el tiempo cura todas las heridas, el tiempo también ha de herir a los que continúen tratando de acuerdo con las convicciones *delayer*.

### RESUME

Comme les autres, l'auteur a pratiquement abandonné l'utilisation du pneumothorax thérapeutique, de la paralysie phrénique, et de la thoracoplastie dans le traitement de la tuberculose pulmonaire. La plupart des malades de son service pour qui un effacement suffisant des lésions n'a pas été obtenue au cours du traitement médical sont alors opérés par résection pulmonaire unilatérale ou bilatérale.

L'auteur préfère l'exérèse pulmonaire à la collapsio-thérapie parce que

- 1) Elle réalise un moyen de traitement plus certain et plus durable
- 2) Elle respecte généralement mieux la fonction respiratoire
- 3) Elle met à l'abri des complications tardives du pneumothorax artificiel et du pneumothorax extra-pleural

4) Elle détermine en général la suppression immédiate de l'expectoration bacillifère

5) Dans l'ensemble, les malades ont besoin d'un traitement infiniment plus court et peuvent être plus rapidement réadaptés

6) Elle permet un mouvement plus rapide d'hospitalisation, corrige l'insuffisance des lits, et rend possible un traitement complet d'une quantité beaucoup plus grande de malades pour une période déterminée

7) L'auteur pense que l'utilisation plus étendue de l'exérèse permettra la réduction du nombre des ré-admissions dues à la rechute et à l'extension de la maladie.

8) Parallèlement on peut obtenir aussi un avantage au point de vue de la santé publique puisque l'infection est plus parfaitement et rapidement jugulée

9) En réduisant le temps consacré au traitement pour chaque malade, on réaliserait une économie très importante à la fois favorable au malade et au pays

L'auteur reconnaît que l'utilisation de l'exérèse est pratiquée trop largement. Il est possible que l'on se rende compte que les médications spécifiques que nous avons maintenant à notre disposition et celles qui vont certainement être encore découvertes permettront de supprimer une grande part de nos indications chirurgicales actuelles. L'auteur a essayé de passer en revue les tendances qu'il a pu décerner dans le traitement chirurgical de la tuberculose pulmonaire, d'après les cas qu'il a vus lui-même

et qui sont probablement comparables à ceux de beaucoup d'autres. Il est nécessaire de remettre en cause à chaque instant nos points de vue.

L'auteur n'a pas cherché à donner des statistiques concernant les résultats du traitement, pensant qu'elles ne peuvent avoir qu'une petite valeur actuellement, étant donné le nombre des cas et le temps écoulé. Il pense que dans quelque dix ans, nous aurons à reconsidérer notre proposition à faire des excisions, exactement comme nous agissons maintenant au point de vue du traitement par le pneumothorax. Car si le temps a la réputation de guérir toutes les plaies, il risque également de causer quelque dommage à ceux que l'on voudrait continuer à guérir selon les procédés qui sont aujourd'hui démodés.

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# Segmental Resection in Pulmonary Tuberculosis\*

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Since 1949, segmental resections for pulmonary tuberculosis have been carried out on a large scale in the Thoracic Centre at Groningen. This follow-up investigation covers 285 patients who had undergone 300 segmental resections, at least six months preceding the date of re-examination. Until November 1, 1954, we performed 490 segmental resections for tuberculosis. No mortality. The first patient was operated upon on November 11th, 1949.

Segmental resection combined with lobectomy, and wedge excision alone, were not included in this series, because the lobectomy cases would probably have exerted an unfavourable influence on the results, while the wedge excision would have made the picture far too optimistic. We did, however, include the results of the combination of segmental resection with wedge excision, because the additional wedge excision is an operation of only minor importance.

During this period, a total of 781 pulmonary resections were carried out for tuberculosis. The numbers of the various types of resection per 100 operations are shown in Table II.

TABLE I  
November 16th, 1949 — August 1st, 1953  
285 Patients (300 simple segmental resections)  
In the same period 781 pulmonary resections were performed in total

Males	179	0-10 years	3
Females	106	11-20 years	35
		21-30 years	143
		31-40 years	73
No mortality, either post-operatively or late		41-50 years	26
		51-60 years	5
		Number	Per Cent
Indications for segmental resection	Tuberculoma	44	14.6
	Caseous foci	168	56
	Cavities (not suitable for non- surgical collapse ther.)	60	20
	Cavities (non-surgical collapse ther. failed)	28	9.33
		300	

The 300 segmental resections were carried out in 285\*\* patients (Tables I and II). Twenty-five of them had bilateral operations. The results of

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(Results of a follow-up of 285 cases in which 300 segmental resections were carried out in the period November 16th, 1949—August 1st, 1953, closing date of follow-up February 1, 1954).

\*\*The patients came from the Bertrix-Ooid Sanatorium at Appelscha (Dr J. K. Kraan), the Military Hospital at Assen (Specialist in Pulmonary Diseases, Dr I. K. Kjaan), the Department for Pulmonary Diseases (Dr N. G. M. Orie) of the Clinic for Internal Diseases, Groningen (Prof Dr F. S. P. van Buchem), the Public Sanatorium at Hellendoorn (Dr H. Vos), and the Roman Catholic Sanatorium 'De Klokenberg' at Tilburg (Dr C. Dijkstra).



TABLE II  
Pulmonary resection for tuberculosis Thoracic Centre, Groningen

	Pneumo- nectomy	Pleu- rectomy	Lobec- tomy	Lobec- tomy + segm re- section	Segm resection	Wedge excision
1-100	61	—	37	—	2	—
101-200	50	—	36	1	13	—
201-300	30	—	29	3	38	—
301-400	17	—	36	4	43	—
401-500	21	—	29	4	44	2
501-600	10	—	18	6	65	1
601-700	9	3	20	4	58	6
701-800	12	1	27	4	55	1
800	210	4	232	26	318	10

the two operations are judged in 15 of these cases, this is not done for the 10 others, because in seven of these the second segmental resection was carried out later than August 1st, 1953, while in the remaining five cases the second operation was lobectomy or wedge excision.

Forty-nine of the 300 segmental resections were combined with wedge excision. The sex ratio of the 285 operation cases was male 179, female 106. The age distribution is given in Table I. As it is our principle to operate only on quiet phthisic foci, which have not healed under bed rest and antibiotics, the great frequency of patients between 20 and 30 is not remarkable.

It must always be considered whether pneumothorax is indicated. At present this is not often carried out in our centre.

When it is a question of choosing between surgical collapse therapy and segmental resection, we prefer the latter, because thoracoplasty, apart from its mutilating nature, is at least as serious an operation. It is an important factor that in thoracoplasty the main focus is not removed, and also that the results of segmental resection are better, both as regards function and sputum conversion. The scheme of treatment in the sanatoria has been modified somewhat since November 1949, due to the introduction of the antibiotics and a better understanding of their action. At present the following is our line of conduct:

(1) The drugs are always given in combination during the rest course (para-aminosalicylic acid, streptomycin, isoniazid INH), in order to obviate resistance.

(2) The following combinations are used:

- (a) PAS 10 g/day by mouth + streptomycin intramuscularly three times weekly 0.5 g, for three months at a stretch
- (b) INH by mouth 4 mg/kg/day + streptomycin intramuscularly, 0.5 g three times per week, usually for a period of 2-3 months
- (c) INH by mouth 4 mg/kg/day + PAS 10 mg/day by mouth, for about three months at a stretch

The three combinations mentioned may be used successively. One prefers combination *a* in fibrocaseous foci, and combination *b* in recent foci.

He does not give more than 1 kg PAS, 30 g streptomycin and 20 g INH

### *Indications for Segmental Resection*

- (1) *Solitary or scattered tuberculoma-like foci* There are various conceptions of "tuberculoma" Our notion of tuberculoma is a round, sometimes slightly ovoid, caseated focus, varying in size from a bean to an apple These encapsulated processes arise because the patient cannot produce sufficient resistance to overcome the process completely, but still enough to prevent further spread

If the tuberculoma is completely quiescent—as manifest by calcification—resection is not strictly necessary, but a regular check-up is sufficient

In all other cases resection of the tuberculoma is the only adequate and safe method of treatment because of the danger of bronchogenic dissemination In some cases operation is decided upon on account of the uncertain diagnosis, although the process seems quiescent

- (2) *Limited non-cavitation processes* which do not heal under conservative treatment The natural resistance of the patient is an important factor when considering whether resection must be employed When the past history shows several relapses and a high familial incidence, we are less inclined to operate

- (3) *Cavitation processes*

(a) One or more cavitation processes, not healing under conservative treatment and less suitable for non-surgical collapse therapy Here we are thinking of cavities in the apical segment of the lower lobe and the hilus, which, as we know from experience, react poorly to collapse The thick-walled cavity and the flooded one are also not suitable for intrapleural pneumothorax

(b) One or more cavitation processes, not healing by conservative treatment and non-surgical collapse therapy

Overholt, Woods and Wilson make a distinction between primary and secondary indications, depending on whether another method of treatment than bed rest or antibiotic therapy has been carried out previously Only the last-mentioned indication is to be considered as secondary in this respect, the other three are primary As bronchiectasis is either the result of a healed tuberculous process (and is then to be included among the ordinary cases of bronchiectasis), or is accompanied by tuberculous foci or cavities, we do not think it necessary to introduce a separate indication for so-called tuberculous bronchiectasis

Table I gives a survey of the frequency of the various indications Among these 300 indications there were three in whom surgical collapse treatment had been carried out previously one had thoracoplasty and two had extrapleural pneumothorax

### *The Pre-Operative Treatment*

The usual precautions in connection with chest operations are observed in segmental resection. Patients are given pre-operatively high doses of vitamins, urine is made alkaline in connection with blood transfusions which may be necessary, and the teaching of respiratory exercises is started at least one week before the operation.

The absolute rest course is interrupted before the operation in order to improve the patient's general condition. One month pre-operatively he is allowed to get up and about for 15 minutes twice daily, after some days this is increased to 30 minutes twice daily.

The pre-operative administration of antituberculous antibiotics is important. It is our practice to give 1 gram of streptomycin daily for a week before operation. In order to suppress common infections, we give about 500,000 U penicillin one or two days prior to the operation.

### *The Operation*

All patients are operated upon in the lateral position, under intratracheal anesthesia with pentothal, nitrous oxide and curare. The thorax is opened with a Crafoord incision or a posterolateral one, followed by subperiosteal resection of the fifth or sixth rib. As a matter of routine the bronchus is searched for first, either via the ventral hilus or the interlobular fissure. The next step is to find the artery and to ligate it. The veins are only ligated in so far as is necessary in the removal of the segment. A clamp is placed on the bronchus, and distally of this clamp the bronchus is severed in stages as far proximally as possible, and closed after each stage with terminal linen sutures. The bronchial stump is always buried carefully, either in the pulmonary tissue or with a purse-string suture under the pleura. In order to retain sufficient pleura for the bronchial stump, the dissection should be done not too far centrally but more peripherally.

The rough pulmonary surface is always pleuralized by suturing the pleural edges of the residual segments. In our opinion, complications, exudations and adhesions are limited in this way. After every segmental resection a single drain is introduced, reaching up to the top of the thorax and emerging at the lowermost point of the pleural cavity in the dorsal axillary line.

The suction pressure exerted on the drain is usually—16 cm  $H_2O$ , it is removed after three to five days.

### *The After-Treatment*

The patient is kept completely supine for the first 24 hours after the operation, and oxygen is administered. Streptomycin is given for two to three weeks. Penicillin is usually stopped one week after the operation. Coughing is considered of high importance. In order to make this less painful, we make full use of analgesics. On the day of operation novocaine is administered via the intravenous drip instituted previously. All pa-

tients operated upon remain in the sanatorium for after-treatment for at least six months and in most cases for seven to eight months

TABLE III  
300 Resected lung segments for tuberculosis

R	134	L	166
<i>Upper lobe</i>	<i>114</i>	<i>Upper lobe</i>	<i>132</i>
anterior segment	5	anterior segment	6
subsegment anterior segment	1	subsegmental anterior segment	3
apical segment	19	apicoposterior segment	85
posterior segment	15	apical subsegment	8
apicoposterior segment	74	posterior subsegment	8
		apicoposterior + anterior segment	14
<i>Middle lobe</i>	<i>0</i>	<i>Lingula</i>	<i>4</i>
<i>Lower lobe</i>	<i>18</i>	superior segment	1
apical segment	6	lingual + anterior segment	3
anterobas segment	1		
cranial subsegment anterior segment	1	<i>Lower lobe</i>	<i>23</i>
laterobas segment	2	apical segment	19
posterobas segment	1	subsegment apical segment	2
lateral + posterobas segment	1	anterobas segment	2
all bas segment	1		
<i>Upper + Lower lobe</i>	<i>7</i>	<i>Upper + Lower lobe</i>	<i>11</i>
apical + posterior segment upper lobe + apical segment lower lobe	6	apicoposterior segment upper lobe + apical segment lower lobe	7
posterior segment upper lobe + apical segment lower lobe	1	anterior + apicoposterior segment upper lobe + apical segment lower lobe	4

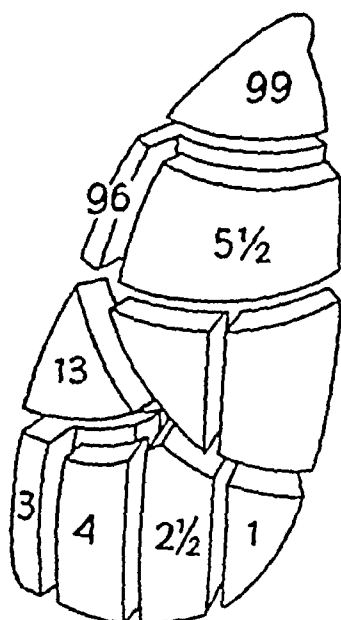
In our series of 300 segmental resections, 418 5 segments were removed altogether, of which 224 were on the right and 194 5 on the left. A subsegment is counted as half a segment, the wedge excisions were left out of consideration. The apical and posterior segments of the right upper lobe count each as one segment, the apical and posterior subsegment of the left upper lobe as a subsegment and the apicoposterior segment as one segment (Tables III and IV give a survey of the number of segments removed). The tuberculous foci suitable for segmental resection are situated mainly in the craniodorsal segments and also fairly frequently in the anterior segment of the left upper lobe and the apical segment of the lower lobe.

Complications and Results

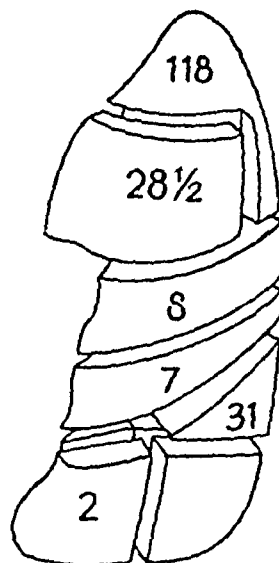
It is often difficult to describe what is meant by the term "complication." We do not call a paresis of the diaphragm due to unavoidable post-operative adhesions a complication, in contrast to a diaphragmatic paralysis—practically always caused by a lesion of the phrenic nerve—which we do consider as such. It is also difficult to say when pleurisy must be called a complication. We took as a criterion the necessity—if any—of thoracic aspiration after the removal of the drain. The difference between pulmonary collapse and atelectasis is based on the extra or intrabronchial character of the causes leading to the falling in of the lung. Pulmonary collapse is radiologically characterized by displacement of the mediastinum to the healthy side and by the presence of fluid or air as an extrabronchial

TABLE IV

**R** 224  
segments removed



**L** 194.5  
segments removed



1 subsegment	= 0.5 segm	in total 418.5 segments were removed in 300 operations in 285 patients
L. apicopost. s.	= 1 segm.	
R apic s.	= 1 segm	
R post. s.	= 1 segm.	

factor of the collapse. In atelectasis the mediastinum is drawn towards the diseased side. The difference between the two is not always easy to recognize, but is of great significance from a therapeutic point of view.

The post-operative course of 127 segmental resections (42.3 per cent) was more or less complicated (78 serious and 49 non-serious complications). Table V gives a survey of the various complications.

Apart from perception deafness, bronchopleural fistula, empyema, reactivation and spread of tuberculosis, complications are not serious and satisfactory treatment is usually possible. Table VI shows the incidence and treatment of bronchopleural fistula. These low figures should not lead to the conclusion that thoracoplasty gives better results than re-resection. This table does, however, demonstrate the favourable effect of thoracoplasty on bronchopleural fistula.

Table VI further shows the incidence and treatment of local encapsulated and diffuse empyemas. The diffuse empyemas were always combined with bronchopleural fistula.

In most cases of bronchopleural fistula with empyema there were, immediately following operation, difficulties concerning the expansion of the lung, without a bronchopleural fistula being demonstrable, however

TABLE V  
127 POST-OPERATIVE COMPLICATIONS

major 78  
minor 49

300 Segmental Resections for Tuberculosis  
(November 16th, 1949—August 1st, 1953)

as per February 1st, 1954  
*no mortality*

### A PULMONARY

	Number	Per Cent		Number	Per Cent
Haemorrhage	11	3 6	Reactivation	9	3
Pneumothorax	11	3 6	(a) homolateral		7*
(a) of short duration		7	(b) heterolateral		2**
(b) tension pneumoth		4	Spread	24	8
Pleuritis (reactive)	33	11	(a) homolateral		21***
Collapse	5	1 6	(b) heterolateral		3****
Atelectasis	30	10	Temporarily positive sputum	2	0 6
(a) of short duration		28	Ulceration bronchial stump	3	1
(b) permanent, partial		2	T B bronchitis	2	0 6
Slow expansion	11	3 6	Post-operative stenosis main bronchus	1	0 3
(a) cured conserv		10	Paralysis diaphragm	7	2 3
(b) thoracoplasty necessary		1	Thrombosis pulm art	1	0 3
Bronchopleural fistula	6	2			
Empyema	8	2 6			
(a) diffuse		6			
(b) partial		2			

\*)  
2 months post-operatively 2  
6 months post-operatively 1  
7 months post-operatively 1  
17 months post-operatively 2  
24 months post-operatively 1

\*\*)   
1 month post-operatively 1  
5 months post-operatively 1

\*\*\*)  
2 months post-operatively 1  
3 months post-operatively 1  
4 months post-operatively 4

5 months post-operatively 2  
7 months post-operatively 1  
8 months post-operatively 2  
9 months post-operatively 1  
10 months post-operatively 1  
12 months post-operatively 2  
14 months post-operatively 1  
16 months post-operatively 1  
18 months post-operatively 1  
20 months post-operatively 2  
27 months post-operatively 1

\*\*\*\*)  
2 months post-operatively 2  
8 months post-operatively 1

### B CARDIOVASCULAR

	Number	Per Cent		Number	Per Cent
Heart complications	2	0 6	Thrombosis leg	5	1 6
(a) irregular pulse		1	Pulmonary embolism	5	1 6
(b) paroxysmal tachycardia		1			

### C NEUROLOGICAL

	Number	Per Cent		Number	Per Cent
Horner	3	1	Plexus arm	4	1 3
Perception deafness (streptomycin)	3	1	(operat. side)		

### D OTHER

	Number	Per Cent		Number	Per Cent
Progressive disease elsewhere (renal t b)	2	0 6	Subcut. emphysema	4	1 3
			Wound suppuration (ligatures)	1	0 3

TABLE VI  
Complications of segmental resection

<i>Results of treatment</i>		
<i>Bronchopleural fistula</i>	6	
Cured thoracoplasty		4
Still under treatment resection		2
<i>Empyema</i>	8	
(a) partial		2
Cured thoracoplasty		1
conserv treatm		1
(b) diffuse		6
Cured thoracoplasty		4
Still under treatment resection		2

In one case the bronchopleural fistula arose a fortnight after the operation, in the other five cases empyema was diagnosed once after one month, once after two months, twice after three months and once after four months. Inadequate technique was presumably an important factor in the first case (No 556), in contrast to the other cases in which probably an important place must be attributed to tuberculous infection of the bronchial stump and (or) the pleural cavity. Incomplete expansion of the lung greatly promotes the development of empyema.

The formation of encapsulated empyemas is probably only based on spread of the tuberculous infection, because one developed seven months and the other two years after the operation.

Table VII gives the incidence and course of reactivation and spread of the pulmonary tuberculosis. These complications especially annul the results of segmental resection. This table once more demonstrates that tuberculosis is a generalized infection and is never removed completely by resection therapy. We believe that the improvement of the results is

TABLE VII  
Complications of segmental resection

<i>Results of treatment</i>			
<i>Reactivation</i>	9	<i>Spread</i>	24
(a) <i>homolateral</i>	7	(a) <i>homolateral</i>	21
<i>Re-resection</i>		Cured	8
still under treatment	5	re-resection	5
<i>Conserv</i>		conserv treatm	3
still under treatment	2	Still under treatment	13
(b) <i>heterolateral</i>		after re-resection	2
<i>Conserv</i>		after thoracoplasty	1
still under treatment	2	conserv treatm	10
		(b) <i>heterolateral</i>	3
		Cured	3
		thoracoplasty	1
		conserv treatm	2

mainly a matter of prevention and combating of spread and reactivation of tuberculosis.

These complications may arise shortly after operation or much later. Homolateral reactivation occurred twice after two months, once after six months, once after seven months, twice after 17 months and once after 24 months. Heterolateral reactivation arose once consequent upon the operation and once after five months.

Homolateral spread was observed once after two months, once after three months, four times after four months, twice after five months, once after seven months, twice after eight months, once after nine months, once after 10 months, twice after 12 months, once after 14 months, once after 16 months, once after 18 months, twice after 20 months and once after 27 months. Heterolateral spread was diagnosed twice after two months and once after eight months.

This proves that operative trauma is not the decisive factor for spread or reactivation of the infection.

*Sputum conversion* see Table VIII. The second and third columns show the number of cases in which good results were obtained after supplementary conservative or surgical treatment alone.

TABLE VIII  
*Sputum conversion 285 patients*  
(300 segmental resections)

Sputum negative 277 = 97.1 per cent		
Immediately after S R	After complem cons therapy	After complem surg therapy
253	11	13
		thoracpl 2 re-resection 11
88.7 per cent	3.8 per cent	4.5 percent

It must, however, be remarked that not all patients with negative sputum are cured, because some of them suffer from spread of the process or reactivation of old lesions.

Table IX shows that the results in cavitation processes are less satisfactory than in tuberculomas or caseated foci, when the cases of sputum conversion are classified according to the indications.

TABLE IX  
*Sputum conversion and indications for segmental resection*  
(300 resections)

Sputum negative 292					Sputum positive 8		
Indication	Immediately after S R		After complem cons therapy	After complem surg therapy	thoracpl	re-resection	
	Number	Per Cent					
Tuberculoma	44	39	88.6	1	2	2	0
Caseous foci	168	155	92.2	7	0	3	3
Cavities	88						
(a) not suitable for non-surg collapse therapy	60	50	83.3	3	0	3	4
(b) non-surg collapse therapy	28	24	85.7	0	0	3	1

Table X proves that the number of patients with negative sputum decreases as time goes on. This is exclusively due to reactivation and spread of the tuberculosis.



TABLE X  
Sputum conversion and observation time  
285 patients (300 segmental resections)

Sputum negative 277							Sputum positive 8
Observation time		Immediately after S.R.	After complem. cons. therapy	After complem. surg. therapy			
		2.1.54	2	thoracopl	re-resection		
4	4 years	2	2	0	0	0	0
3	—3 years	33	26	3	1	3	0
2	—2 years	88	75	6	1	4	2
1	—1 years	110	101	2	0	3	4
1	year—6 months	52	49	0	0	1	2

Table XI shows the number who have resumed their work completely or partially or will be able to do so in the near future. The future, as regards fitness for work, remains problematic for 9.1 per cent. All who were not yet completely fit for work on the date of re-examination (February 1, 1954), will—apart from unexpected circumstances—resume their work completely in the near future.

TABLE XI  
Segmental resection *t b c*  
285 patients  
per February 1st, 1954

Able to work			
100% fully active life	half-time job	at work in the near future	not yet decided
199	15	14	26
69.7 per cent	5.2 per cent	15.7 per cent	9.1 per cent

Investigation of pulmonary function has shown that after segmental resection the average loss of vital capacity is 348 ml, of maximum respiratory minute volume 57 l, of C.U.S. (Tiffeneau) ml, of vital capacity and oxygen uptake on the operated side 5.3 per cent and 6.2 per cent respectively.

When the results of the pulmonary function tests agree with these values, we speak of a normal functional loss caused by the operation. When the values have fallen unduly, the loss is considered too great (Table XII).

TABLE XII  
Pulmonary function tests at least six months after segmental resection for tuberculosis in 222 of the 285 patients

Normal loss		Loss of function too great	
173		49	
77.9%		22%	
Paresis diaphr	12	Slow expansion	3
Paralysis diaphr	7	Empyema + br pl fistula	5
Pleuritis	7	Thrombosis pulm. art.	2
Pneumoth	3	Operative damage	
Atelect	2	pulm. art	1
Collapse	1	Cause ??	8
Haemothor	1		

Causes for too great a loss were paresis of the diaphragm in 12 cases and paralysis of it in seven. Pleurisy was a harmful factor in seven, post-operative pneumothorax three, atelectasis two, pulmonary collapse once, hemothorax once, delayed expansion three and empyema with bronchopleural fistula five times. In two the cause of the bad pulmonary function was thrombosis of the pulmonary artery, and once operative trauma of this artery. In eight no cause was found for the abnormal reduction in pulmonary function. A remarkable feature is that in four of post-operative hemorrhage the pulmonary function improved following streptokinase/streptodornase treatment.

TABLE XIII  
300 Segmental resections  
November 16th, 1949—August 1st, 1953  
*Results of operation, and observation time*

			Good 248 81 per cent	Moderate 18 6 per cent	Bad 39 13 per cent
	4 years	2	2 (100 )	0	0
4	—3 years	33	22 ( 66 6)	4	7 (21 2)
3	—2 years	89	71 ( 79 7)	4	14 (16 6)
2	—1 years	121	98 ( 80 9)	9	14 (11 5)
	1 year—6 months	55	50 ( 90 9)	1	4 ( 7 2)

All bilateral resections were good except in one with spread after his second S R. The first S R had been recorded as 'good', the second as 'bad' (Nos 701 and 762).

Table XIII gives the total results of segmental resection. The result is considered moderate when the main object of the operation, i.e., the returning to useful life of a healthy person with negative sputum, is indeed attained, but that complications not requiring surgical treatment have affected the general or local state of the patient to a greater or lesser degree. Moderate results were caused seven times by paralysis of the diaphragm, five times dyspnoea arose when the patient did somewhat heavier work, and three times perception deafness occurred due to streptomycin.

Tension pneumothorax, hemothorax, unsatisfactory expansion of the lung, encapsulated empyema and transient positive sputum were also of importance, without an explanation being found for it.

We speak of *bad* results when the main purpose of segmental resection has not been reached, or when the general or local condition is seriously affected due to complications. Spread or reactivation was in 32 cases the cause of failure of segmental resection (in one both spread and reactivation), six times diffuse empyema and once encapsulated empyema which was treated by thoracoplasty. The latter operation was also necessary in one patient because of insufficient expansion of the lung. The moderate results were largely due to faulty technique. The bad results were largely due to spread or reactivation after the tuberculous pulmonary process.

Even more than is the case with sputum conversion, the results in patients with cavities are worse than in those with caseated foci and tuber-

culomata Table XIII shows that just as in sputum conversion the results of segmental resection become less good with increasing duration of the observation period. It seems therefore premature to pass a definite judgment on the value of segmental resection.

Table XIV gives the number of patients cured after segmental resection alone, or after this operation combined with supplementary conservative or surgical treatment. The prognosis was doubtful to bad for only 1.4 per cent of those not yet cured.

TABLE XIV  
Follow-up of 285 patients  
(300 segmental resections for tuberculosis per February 1st, 1954)

Cured 262 (92 per cent)			Still under treatment 23 (8 per cent)	
by S R alone	by S R with supplement- ary conserv- treatment	by S R with supplement- ary surgical treatment	Prognosis doubtful to favourable	Prognosis doubtful to bad
		Re-resection 5 Thoracopl 4		
246	7	9	19	4
86.3 per cent	2.4 per cent	3.1 per cent	6.6 per cent	1.4 per cent

#### SUMMARY AND CONCLUSIONS

- 1 The post-operative course of 300 segmental resections in 285 patients with tuberculoma, localized caseated foci or cavitational processes was complicated in 127 (42.3 per cent). Most of the complications were of an innocent or transient nature.
- 2 In three cases perception deafness occurred consequent upon the routine streptomycin treatment (maximally 20 g). Apart from two encapsulated empyemata which were cured, six diffuse empyemata with bronchopleural fistula were observed. Four of them recovered after thoracoplasty, and two are still under treatment after re-resection. Reactivation of the pulmonary tuberculosis occurred in nine, spread in 24 patients. All cases of reactivation are still under treatment. Eleven with spread have already recovered, either after conservative or after supplementary surgical treatment.
- 3 At the follow-up examination 97.1 per cent of patients had negative sputum. The results were better in the cases of caseated foci and tuberculomata than in cavitational processes. The percentage of negative sputum decreases somewhat with increasing duration of the observation time.
- 4 More than 90 per cent have resumed their work or will do so in the near future.
- 5 In nearly 80 per cent loss of pulmonary function was no greater than was to be expected after segmental resection.
- 6 Of those who had undergone segmental resection 92 per cent were

cured at the time of re-examination, which was at least six months after the operation. For only 14 per cent the prognosis was doubtful to bad.

- (7) The final result of segmental resection was good in 81 per cent of cases. The results were here also better for tuberculomata and caseated foci than for cavitational processes. The number of good results decreases with increasing time of observation.
- (8) Up to February 1, 1954 there was no fatal case among the series discussed, either post-operatively or during follow-up.

### RESUMEN

1 La evolución postoperatoria de 300 resecciones segmentarias en 285 enfermos con tuberculoma, focos localizados caseosos o procesos cavitarios, se complicó en 127 (42.3 por ciento). La mayoría de las complicaciones fué de naturaleza transitoria e intrascendentes.

2 En tres casos ocurrió sordera de percepción después del uso de rutina de estreptomycin (máximo 20 grms). Fuera de dos empiemas encapsulados que se curaron, se observaron seis empiemas difusos con fístula broncopleural. Cuatro de ellos se recuperaron después de toracoplastia y dos están aún bajo tratamiento después de re-resección. La reactivación de la tuberculosis pulmonar ocurrió en nueve y la diseminación en 24 enfermos. Todos los casos de reactivación están aún bajo tratamiento. Once casos con reactivación se han recuperado ya sea por medios conservadores o después de tratamiento quirúrgico suplementario.

3 Según la prosecución de los enfermos, 97.1 de los enfermos tuvieron esputos negativos. Los resultados fueron mejores en los casos de focos caseosos y en los tuberculomas que en los procesos excavados. El porcentaje de esputos negativos decrece algo al aumentar el tiempo de observación.

4 Más del 90 por ciento han vuelto a su trabajo o lo harán en el futuro próximo.

5 En casi el 80 por ciento la pérdida de la función pulmonar no fué mayor de lo esperado después de resección segmentaria.

6 De los que sufrieron resección segmentaria, 92 por ciento estaban curados al ser re-examinados, lo que fué por lo menos seis meses después de la operación. Solamente para el 14 por ciento el pronóstico fué dudoso o malo.

7 El resultado final de la resección segmentaria fué bueno en 81 por ciento de los casos. Los resultados fueron también mejores para los tuberculomas y los focos caseosos que para los excavados. El número de buenos resultados disminuye al aumentar el tiempo de la observación.

8 Hasta el 1 de Febrero de 1954, no ha habido un caso fatal en la serie que se discute, ya sea postoperatoriamente o durante la prosecución.

### RESUME

1 Les suites opératoires de 300 résections segmentaires pratiquées chez 285 malades pour tuberculome fover caséux localisé, ou lésion

cavitaire, furent l'objet de complications chez 127 d'entre eux (42,3%) La plupart de ces complications furent bénignes et éphémères

2 Dans trois cas, une surdité apparut, à la suite du traitement systématique par la streptomycine En dehors de deux pleurésies purulentes enkystées, qui furent traitées, qui furent traitées, on observa six cas de pleurésie purulentes avec fistule bronchopleurale Quatre d'entre elles guérirent après thoracoplastie et deux sont encore actuellement en traitement après une nouvelle exérèse Une rechute de la tuberculose pulmonaire survint chez neuf malades et un ensemençement chez 24 Tous les cas de rechutes sont actuellement en cours de traitement Onze cas qui avaient eu des propagation à distance ont complètement guéri, soit par le simple traitement médical, soit après une nouvelle intervention chirurgicale

3 Lors de l'examen complet, 97,1% des malades avaient négativé leur expectoration Les résultats furent supérieurs dans les cas de foyer caséux et de tuberculome à ceux où il existait une cavité Il y eut une certaine diminution du pourcentage des expectorations négatives, à mesure qu'augmenta le temps d'observation

4 Plus de 90% des malades ont repris leur occupation professionnelle ou sont sur le point de le faire

5 Dans près de 80% des cas, on n'a pas eu à déplorer une diminution de la fonction pulmonaire supérieure à ce qu'on peut attendre à la suite d'une résection segmentaire

6 Parmi les malades qui ont subi une résection segmentaire, 92% se montrèrent guéris lors d'un nouvel examen qui fut pratiqué au moins six mois après l'opération Ce n'est que dans 1,4% des cas que le pronostic était douteux ou mauvais.

7 Le résultat final des résections segmentaires se montra favorable dans 81% des cas Les résultats là aussi furent meilleurs pour les tuberculomes et les foyers caséux que pour les foyers cavitaires La quantité des résultats favorables diminua à mesure qu'augmentait le temps d'observation

8 A la date du 1er février 1954, il n'y eut aucune mortalité parmi les cas qui sont étudiés, soit après l'opération, soit au cours de la surveillance consécutive

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# Intrapleural Enzymatic Debridement With Tryptar

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Of the various complications which may occur as a result of pulmonary tuberculosis, thoracic empyema has always been one of the most difficult to successfully combat. All physicians experienced in the treatment of this condition can recall the numerous aspirations, pleural lavage and drainage procedures frequently required and the usually futile attempts to obliterate the infected pleural space and re-expand the lung.

Sterilization of the space became possible in certain instances with the increased use of the various antibiotic drugs. This procedure per se, however, could not usually produce a cure because of the inability of the lung to re-expand as a result of the thick, fibrous membrane holding it captive. Extensive thoracoplasty was often resorted to in an effort to appose the chest wall to the unexpandable lung and thereby obliterate the empyema space. Surgical decortication of the inflammatory peel was applied to cases of tuberculous fibrothorax following the successful results obtained by this form of treatment when used in non-tuberculous conditions. The results with decortication in the tuberculous group were less successful than in non-tuberculous cases because of the inability to sterilize the empyema space preoperatively.

Reiser, Roettig and Curtis<sup>1</sup> approached this problem by utilizing the pancreatic enzyme trypsin as a debriding agent. This substance was injected into the empyema cavity in an effort to digest the shaggy, pyogenic membrane by its proteolytic action, hoping the raw infected surface thereby exposed might be made amenable to treatment by antibiotic drugs. By controlling the infection, decortication could be made a safer and more successful procedure. Of the initial six cases of mixed tuberculous empyema reported by these authors, two obtained a complete cure of empyema using trypsin alone, while the others showed a decrease in viscosity and clearing of the fluid. Positive fluid became negative in four instances. An additional 10 cases were reported by Roettig, Reiser, Habeeb and Mark<sup>2</sup> in March, 1952, with similar good results.

*Action of Tryptar* These workers<sup>1, 2</sup> have studied the action of trypsin *in vitro* and *in vivo* and have noted the rapid liquefaction of fibrin clots and decrease in viscosity of the empyema fluid. Crystalline trypsin injected intrapleurally in dogs causes prompt pleural effusion which resolves within one week leaving no detectable residual pleural reaction. It will also digest other dead tissue such as muscle, blood vessels, skin and fascia, but will not attack living cells. This is of considerable importance and denotes the relative safety in using trypsin as compared to the proteolytic enzymes of streptococcal origin against which the body has no

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Material used in the study was tryptar, a pure crystalline trypsin, supplied by The Armour Laboratories.

Presented at the annual meeting of the Southern Trudeau Society, (Miami Beach, Florida) September 12, 1952.

protective anti-enzyme The fibrin and viscid nucleoprotein of the pyogenic membrane are readily digested leaving exposed a raw, clean pleural surface Empyema fluid changes in character from a thick pus to a thin, watery, slightly turbid fluid which eventually becomes amber or straw-colored Grossly bloody changes are noted after several days of treatment and indicate debridement of the inflammatory membrane and action of the trypsin on the exposed pleural surface

In the majority of cases, pleural fluid becomes bacteriologically negative on smear and culture for acid-fast and other organisms It is believed that trypsin in itself is not bactericidal but causes sterilization of the space through its debriding action by depriving bacteria of culture media needed for growth.

*Side Effects* A histamine-like reaction has been noted when trypsin is administered parenterally Transient temperature elevation and increase in the pulse rate occur Slight hypotension may be noted Administration of an anti-histaminic prior to the use of trypsin will protect against these manifestations Pain may occur when trypsin comes in contact with the healthy pleural surface No instance of severe sensitivity produced by the preparation has been noted

Results obtained by Roettig, Reiser, Habeeb and Mark were so promising as to encourage other workers to employ this method in the treatment of empyema Only one of their 17 cases could be classed as a complete failure Six cases showed re-expansion of the lung using tryptic alone In all of these cases, empyema had been present for a period of less than six months prior to treatment In the remaining cases, success was measured in terms of rapid decrease in the viscosity of the empyema fluid, lysis of the pyogenic membrane and sterilization of the space Some of these cases went on to complete cure through supplementary surgical procedures such as decortication Results were more satisfactory in the non-tuberculous or mixed infections Subsequent direct inspection of the pleura in five cases showed it to be clean and glistening Viscosity of the empyema fluid decreased in all 17 cases and sterilization of the space was noted in 12 of the 13 instances in which organisms had been present prior to treatment The average time required for this conversion was 10 days

Although the occurrence of bronchopleural fistula was not noted following the use of trypsin, this eventuality must be kept in mind when enzymatic debridement is employed in the immediate postoperative period Its use postoperatively should probably be withheld until bronchial healing has occurred McCloskey and Hardin<sup>3</sup> used tryptic debridement in the treatment of clotted hemothorax two weeks following spontaneous rupture of a syphilitic aneurysm of the ascending aorta Thoracotomy was subsequently performed and revealed the point of rupture of the aortic aneurysm was sealed over by adherent lung Trypsin had produced an effective lysis of the clotted hemothorax but apparently did not interfere with the reparative process between the lung and the ruptured aneurysm

Following the lead of Roettig and his co-workers, the author was encouraged to use this method of treatment in certain instances of tuber-

culous, non-tuberculous and mixed infection empyema The technique of treatment varied somewhat in the fact that an indwelling number 16 French catheter intercostal tube was used in most of the present cases The tube was clamped for eight to 12 hours following instillation of the trypsin and was connected to a negative pressure suction apparatus when reopened Patients were instructed to change position frequently Bena-dryl, 50 mg, was given before each treatment and as required subsequently The trypsin used was tryptar, a pure crystalline trypsin

### Case Reports

*Case 1* F M, a 31 year old white female, was seen on November 2, 1951, with left tuberculous empyema, the result of an unexpanded therapeutic pneumothorax The patient had been under treatment for tuberculosis intermittently since 1947 with periods of sanatorium care, streptomycin and para-aminosalicylic acid, pneumothorax and aspirations of pleural effusion Therapeutic pneumothorax had been instituted in July, 1950, and thin, clear pleural effusion was noted in October, 1950 The fluid remained thin and small in quantity until the fall of 1951 Left thoracentesis on November 8, 1951, yielded thick, yellow pus which was positive for acid-fast bacilli on smear and culture, but negative for other organisms X-ray film at this time showed the left lung to be 50 per cent collapsed and held captive by a 3-4 mm in-

FIGURE 1



FIGURE 2



*Figure 1*—Case 1 Tuberculous empyema, left Roentgenogram prior to treatment with tryptar *Figure 2*—Case 1 Tuberculous empyema, left Roentgenogram following second instillation tryptar Intercostal tube in place



flammatory peel The pneumothorax space was approximately 50 per cent filled with fluid Following admission to the Tampa Municipal Hospital a number 16 French catheter was inserted into the left third interspace for the purpose of closed drainage and 250 cc of pus were evacuated after which 250,000 units of tryptar dissolved in 25 cc of Sorensen's phosphate buffer solution were instilled through the tube which was then clamped off for a 12 hour period This procedure was repeated daily for four days Upon each occasion, the chest tube was connected to the suction apparatus for several hours prior to instillation of tryptar Thick coagulum and proteolytic debris could be noted returning through the tubing on each occasion and by the end of 48 hours the thick pus had changed in consistency to a thin, white, turbid fluid Long membranous strands were found in the bottom of the drainage bottle representing desquamated inflammatory peel A pinkish tinge to the fluid was noted following the third instillation X-ray film at the end of 48 hours showed the lung to be approximately 90 per cent expanded Six days following the first course of 1,000,000 units, a second course was given, again consisting of four daily administrations of 250,000 units each This was done in an effort to obliterate a small residual space The intercostal tube was removed Smear and culture for acid-fast bacilli were negative on the 10th day following the initial instillation of tryptar

Since treatment, the lung has remained expanded and there has been no evidence of the recurrence of the empyema In this instance it appeared that the most significant benefit from tryptic debridement occurred during the first few days of treatment.

*Case 2* J G, a 34 year old white male, was admitted to the Southwest Florida Tuberculosis Hospital on November 3, 1951, for his fifth period of sanatorium care Pulmonary tuberculosis was first diagnosed in May, 1945 Therapeutic left pneumothorax was instituted in August, 1948, and continued until July, 1950, at which time it was abandoned due to fluid accumulation and spread of disease to the right lung Fluid was aspirated from the left chest with fairly good re-expansion of the lung Right pneumothorax was thereupon initiated and continued for nine months at which time it became necessary to discontinue because of occurrence of spontaneous pneumothorax following a refill

At the time of the present admission, the right lung had completely re-expanded but there was noted a 50 per cent collapse of the left lung and the presence of a fluid



FIGURE 3—*Case 1* Tuberculous empyema, left Final result following enzymatic debridement with tryptar

level Grossly purulent fluid (800 cc) was removed on January 21, 1952, and a number 16 French catheter was inserted into the left pleural cavity, sixth intercostal space, posterior axillary line, and connected to the negative pressure suction apparatus. The fluid was positive on culture for acid-fast organisms. Tryptar, 250,000 units, was introduced through the chest tube on four occasions, January 21, 22, 24 and 26, and left in the pleural space for a period of eight to 12 hours on each occasion, the chest tube being clamped off during this period. The empyema fluid became progressively thinner and tended to lose its grossly purulent character. Re-expansion of the lung occurred and the chest tube was removed. The lung has remained expanded in this case with no evidence of recurrence of fluid formation.

Although the left pneumothorax and pleural effusion in this case were of several

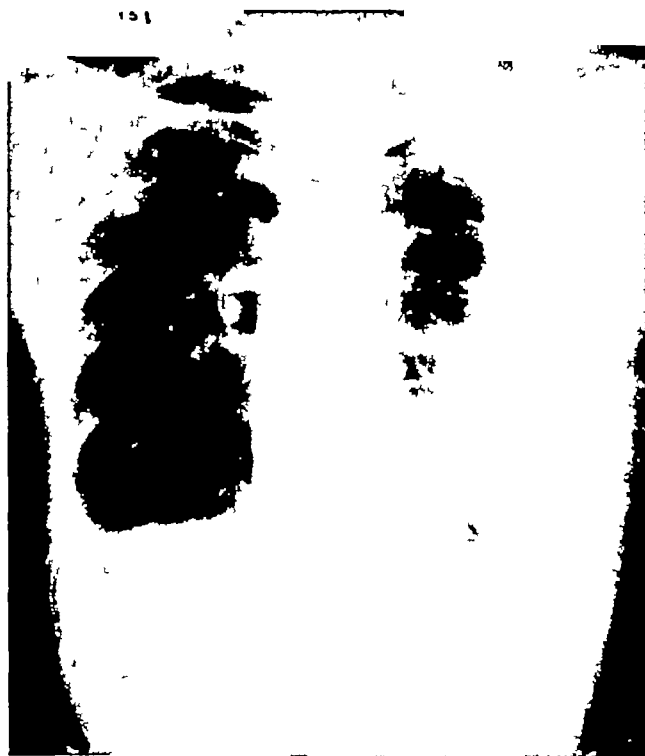


FIGURE 4—Case 2 Tuberculous empyema, left Roentgenogram prior to treatment with tryptar



FIGURE 5—Case 2 Tuberculous empyema, left Roentgenogram following fourth installation of tryptar. Intercostal tube in place

year's duration, the empyema was probably of rather recent origin. This case represents what appears to be a rather rapid cure of a tuberculous empyema.

*Case 5* E P, a 34 year old white female, had her apparent onset of tuberculosis in July, 1951. She was hospitalized at the Southwest Florida Tuberculosis Hospital on September 18, 1951, when sputum was positive for acid-fast bacilli. A course of streptomycin and para-aminosalicylic acid was given. On February 19, 1952, the apical-posterior segment of the left upper lobe was removed. The operation was uneventful, but failure of complete re-expansion occurred postoperatively and a residual apical space persisted. On March 10, 1952, 21 days postoperatively, an intercostal tube was placed in the first anterior interspace, left, and connected to the continuous negative suction apparatus. The lung still failed to re-expand completely and the tube was removed on March 18, 1952. On March 28, 1952, chest aspiration yielded purulent fluid. Culture of the fluid produced staphylococcus and gram negative bacilli, probably proteus. These organisms were resistant in vitro to penicillin, bacitracin, streptomycin, chloromycetin, aureomycin and terramycin. No acid-fast bacilli were cultured.

At the time of this aspiration, tryptar, 250,000 units, was placed within the empyema space. This was repeated daily for four consecutive days with progressive clearing and decrease in viscosity of the fluid. After a lapse of one week, a small amount of residual fluid and air space persisted and the same dosage was again administered on two occasions three days apart.

The patient has remained well and, although an apical cap persists on x-ray inspection, fluid can no longer be obtained on aspiration. She has subsequently been discharged as arrested.

*Case 4* V W, a 38 year old white female, had been treated intermittently since 1941 for pulmonary tuberculosis. Left therapeutic pneumothorax was instituted in 1942 and continued until the present time. In January, 1951, left pleural effusion developed and was treated by means of periodic aspiration. She was admitted to the Southwest Florida Tuberculosis Hospital in January, 1952, by which time the pleural effusion had become purulent. Culture was positive for *Staphylococcus aureus*, but negative for tubercle bacilli.

An intercostal tube was inserted in the first interspace anteriorly and connected to the suction apparatus. Two courses of tryptar were administered consisting of one

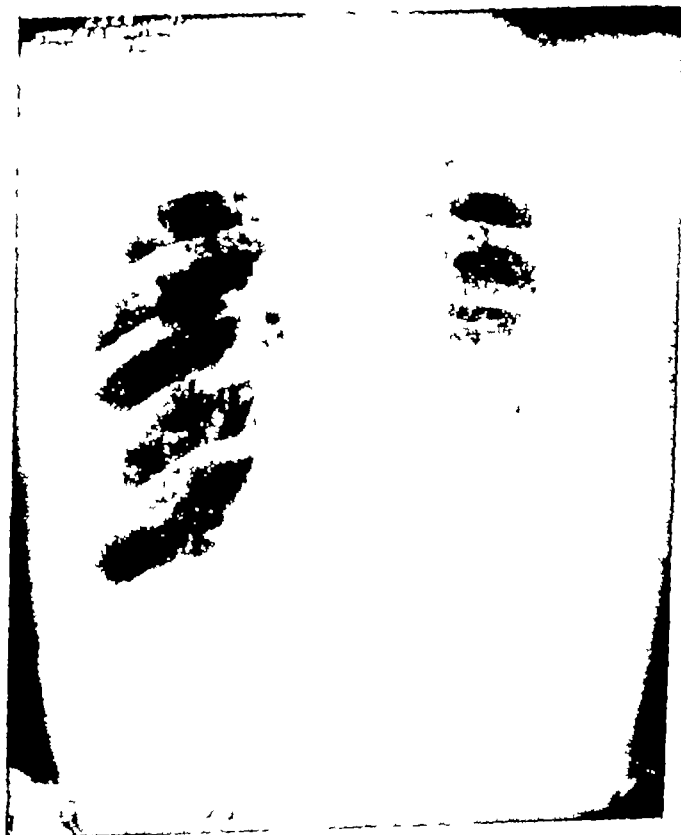


FIGURE 6—*Case 2* Tuberculous empyema, left. Roentgenogram one month following completion of treatment with tryptar. Pleural space obliterated.

million units each. For the first course, 250,000 units per injection were given on March 13, 14, 16 and 18. The tryptar was left in the chest with the tube closed for periods ranging from eight to 12 hours when the chest tube was again connected to the negative pressure suction machine in an effort to remove the fluid and debris and re-expand the lung. The fluid became somewhat less viscid in character, but still remained grossly purulent. After the third injection, the fluid was blood-tinged. Re-expansion of the lung did not occur. The second course of tryptar consisted of 250,000 units, given on April 20, 21, 22 and 23. The lung did not re-expand. No growth of organisms was obtained, however, following the first course of tryptar. In retrospect, one could probably not hope for re-expansion in this case, the condition having been in existence for a period considerably in excess of the six month limit defined by Roettig, Reiser, Habeeb and Mark.

Severe headache, malaise and temperature elevation to 100 to 101° F followed each instillation of the tryptar in this case, the reaction eventually being controlled by the administration of benadryl prior to the tryptar and subsequently as required.

Surgical decortication was eventually required in this patient and was performed on September 2, 1952. It is felt that tryptar materially added to the safety of decortication by its sterilizing action on the pleural fluid. A third series of eight injections of tryptar (250,000 units each) was administered just prior to surgery.

*Case 5* F W, a 37 year old white female, was known to have had tuberculosis since 1949. Following a year of sanatorium care during 1950-1951 and treatment with streptomycin and pneumoperitoneum, she was discharged. In October, 1951, left spontaneous pneumothorax occurred which rapidly progressed to hydropneumothorax and empyema. On admission to the Southwest Florida Tuberculosis Hospital on December 5, 1951, the left chest fluid was grossly purulent and positive on culture for acid-fast bacilli, *B. pyocyaneus* and hemolytic *Staphylococcus albus*. X-ray film at that time suggested a destroyed left lung with associated empyema. Because of the fluid, however, lung detail could not be seen satisfactorily. Despite the probable extensive, underlying pulmonary pathology, it was decided to attempt a trial of enzymatic debridement with tryptar. Accordingly, eight instillations of 250,000 units each (total 2,000,000 units) were administered on successive days following the insertion of an intercostal tube in the left third intercostal space, anterior axillary line. Tryptar was left in the space for eight to 12 hours on each occasion after which suction was applied to the chest tube.

No notable re-expansion of the lung occurred in this case, and none could be expected in view of the underlying pulmonary disease. Temporary decrease in the viscosity of the fluid was noted and no growth of organisms was obtained following completion of the series of treatments with tryptar.

Obliteration of the pleural space readily occurred following open drainage and she has subsequently been rehabilitated by Schede thoracoplasty. It is felt that instillation of tryptar contributed materially to the good result obtained.

*Case 6* G S, a 26 year old white male, was seen in consultation on May 19, 1952, with a history of insidious onset of bilateral pleural effusion, pericardial effusion, dyspnea and chest pain. It had become necessary to aspirate each pleural space at



FIGURE 7

FIGURE 8

*Figure 7—Case 3* Non-tuberculous empyema following segmental resection for tuberculosis. Roentgenogram prior to treatment with tryptar. *Figure 8—Case 3* Non-tuberculous empyema following segmental resection for tuberculosis. Roentgenogram following enzymatic debridement with tryptar.

ternately every two or three days at which time a liter or more of clear, straw-colored fluid was withdrawn with temporary relief of dyspnea. This procedure had been carried out for a period of about three weeks with no evidence of decrease in the amount of fluid formation. The fluid was negative on all examinations for malignant cells, acid-fast and other organisms, and fungi. No growth of organisms was obtained at any time. Physical examination, except for the chest, and other laboratory tests, including agglutinations, were all within normal limits. Biopsy of an enlarged cervical lymph gland was also negative.

Despite the puzzling nature of this case and our inability to diagnose the underlying cause of the polyserositis, it was felt mandatory to in some way combat the excessive pleural effusion and associated protein loss and discomfort to the patient. Accordingly, a number 16 French catheter was inserted first into the left pleural cavity through the ninth intercostal space, mid-axillary line and connected to the continuous suction apparatus. The tube was left in place for four days. Fibrin balls and sediment plugged the tube. It was decided to instill tryptar with two objectives in mind, to proteolyze the sediment allowing better drainage of fluid and perhaps irritate the pleural surfaces sufficiently to cause symphysis, thus arresting the formation of pleural fluid. This result was realized. Following removal of the chest tube, the pleural pocket was no longer noted and aspiration of a small amount of fluid from the left chest was required on only one subsequent occasion.

It was decided to carry out a similar procedure on the right side and this was accomplished with similar good results, although somewhat more time was required than on the left side.

Just how much credit can be given to tryptar in this case is difficult to evaluate. The same result might have been obtained by intercostal drainage alone. Tryptar, 250,000 units, was instilled only once on each side. Following this, on each occasion, he experienced malaise, rather severe chest pain on the side of the injection and moderate elevation of temperature. The pleural fluid became pink, indicative of tryptic action on the raw pleural surface.

*Case 7* E. T., a 32 year old white female, developed pulmonary tuberculosis in July, 1945. Since that time, most of her life had been devoted to the treatment of this condition in and out of various sanatoria. Treatments included bilateral pneumothorax, antibiotic therapy, left thoracoplasty (1947), and right extrapleural pneumothorax (1948). She did well until March, 1952, at which time she developed fluid in the right extrapleural space which soon became purulent. This was treated by open drainage in April, 1952, and a tube has remained in place until the present time. Admission to W. T. Edwards Tuberculosis Hospital, Tallahassee, Florida, was on June 24, 1952.

On August 15, 1952, a course of tryptar was given consisting of 10 daily injections of 250,000 units into the right extrapleural space. A marked decrease in the viscosity and purulent character of the drainage was noted, but complete lung re-expansion did not occur. The drainage material was blood-tinged on several occasions. Some difficulty was experienced in retaining the tryptar because of the open drainage. Plugging the drainage tract with gauze was attempted.

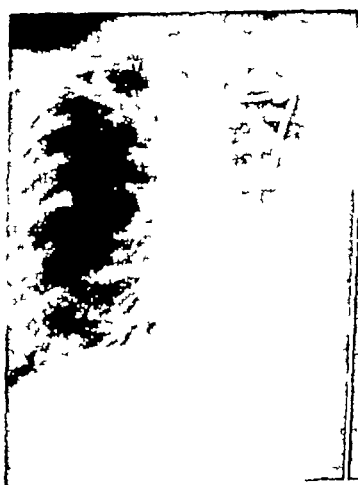


FIGURE 9



FIGURE 10



FIGURE 11

*Figure 9*—Case 4. Post-pneumothorax empyema with intercostal tube in place preparatory to treatment with tryptar. *Figure 10*—Case 4. Post-pneumothorax empyema. Failure of re-expansion following use of tryptar but sterilization of the space prior to surgical decortication. *Figure 11*—Case 4. Post-pneumothorax empyema. Roentgenogram subsequent to uncomplicated surgical decortication.

Although there was improvement in general well-being and a decrease in toxicity in this patient, as well as improvement in the character of the empyema fluid, results can not be classified as successful. The fact that the upper part of the lung had been compressed for four years with associated fibrosis and contraction would naturally mitigate against the possibility of re-expansion by tryptar in this case. Improvement, therefore, can only be measured in terms of decreased viscosity and sterilization of the fluid.

*Case 8* A H, a 43 year old colored male, underwent right upper lobectomy for a post-pneumonia chronic lung abscess at Tampa Negro Hospital on August 6, 1952. The surgical procedure and immediate convalescence were uneventful. On the 12th postoperative day the presence of bronchopleural fistula was suspected and within 48 hours a definite diagnosis of empyema was established. He was coughing up thick dark material characteristic of bronchopleural fistula and the chest x-ray film revealed a large right upper empyema space with a fluid level. Thick brown pus was aspirated from the post-resection space, this fluid being negative for growth of organisms on culture, probably as a result of intensive pre- and postoperative antibiotic therapy.

Despite the presence of an obvious bronchopleural fistula, it was decided to treat with tryptar through closed intercostal drainage. A number 16 French catheter was inserted into the empyema space in the anterior right first interspace, mid-clavicular line, and connected to the continuous negative pressure suction apparatus. 250,000 units of tryptar were instilled through the tube daily which was then clamped off for a period of eight to 12 hours to allow for maximum effect of the enzyme. Prior to injection of tryptar, the space was irrigated with saline on each occasion until returned clear. Tryptar instillation was performed for eight consecutive days with progressive thinning and decrease in the viscosity of the fluid as well as re-expansion of the remaining middle and lower lobes with obliteration of the space. Organisms were not cultured at any time.

This case must be classed as non-tuberculous empyema inasmuch as the tubercle bacillus was never demonstrated during his pulmonary ailment prior to surgery or subsequently. The rapid cure of postoperative empyema which may be expected following the use of tryptar is well demonstrated by this case. The presence of a bronchopleural fistula did not appear to contraindicate its use and this readily closed during the course of tryptar therapy.

#### SUMMARY AND CONCLUSIONS

The cases presented illustrate some of the situations in which the pancreatic enzyme trypsin can be used for the purpose of selective intra-

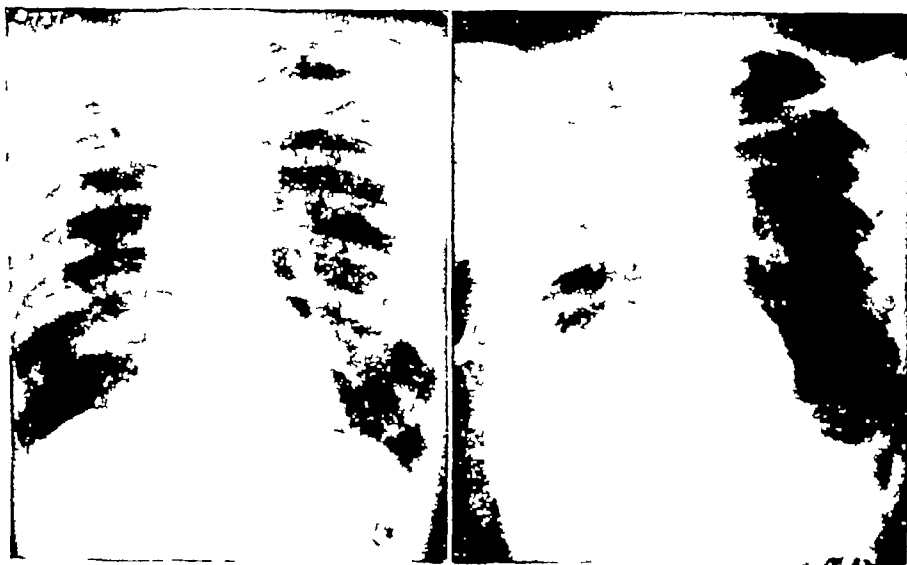


FIGURE 12

FIGURE 13

*Figure 12*—*Case 8* Lung abscess right upper lobe. Preoperative roentgenogram.  
*Figure 13*—*Case 8* Lung abscess. Roentgenogram subsequent to right upper lobectomy complicated by broncho-pleural fistula and empyema. Intercostal tube in place for closed drainage and instillation of tryptar.

pleural proteolytic debridement. These included tuberculous empyema, tuberculous infection of the extrapleural space, mixed tuberculous empyema, non-tuberculous empyema following resection for tuberculosis, non-tuberculous postoperative empyema, and non-specific bilateral pleural effusion of an indeterminate nature.

Complete cure was obtained in the two cases of tuberculous empyema and the two cases of postoperative empyema, and almost complete relief obtained in the case of bilateral effusion of unknown origin. Improvement as manifested by decrease in viscosity and sterilization of the fluid was noted in the other three cases and contributed to eventual good surgical results in this manner. Following these initial encouraging experiences, tryptic debridement has subsequently been employed in an additional 22 patients with comparable results. In addition to the above mentioned indications, this method has been successfully used in the treatment of postoperative and traumatic hemothorax.

It is concluded that tryptic debridement is a valuable adjunct in the treatment of intrapleural infections and hemothorax and is deserving of more widespread usage. Side effects are few and inconsequential. Its use is not necessarily contraindicated in the presence of bronchopleural fistula.

#### RESUMEN

Los casos que se presentan ejemplifican algunas de las condiciones en que la enzima tripsina pancreática, puede usarse para obtener la desbridación proteolítica intrapleural selectiva. Tales condiciones incluyen el empiema tuberculoso, la infección tuberculosa del espacio extrapleural,



FIGURE 14—Case 8. Lung abscess. Final roentgenogram following removal of tube and re-expansion of lung with healing of broncho-pleural fistula and obliteration of the empyema space.

el empiema mixto tuberculoso, el empiema no tuberculoso después de resección por tuberculosis, el empiema postoperatorio no tuberculoso y el derrame pleural bilateral no específico, de naturaleza indeterminada.

Se obtuvo una cura completa en dos casos de empiema tuberculoso y en dos casos de empiema postoperatorio, un alivio casi completo se obtuvo en el caso de derrame pleural bilateral de naturaleza desconocida. Se notó la mejoría por el decrecimiento de la viscosidad y la esterilización del líquido se notó en los otros tres casos y contribuyó a los buenos resultados quirúrgicos logrados.

Después de estos alentadores iniciales la desbridación triptica se empleó en otros 22 enfermos con resultados comparables. Además, de las indicaciones ya mencionadas este método se ha empleado con éxito en el tratamiento del hemotórax postoperatorio y traumático.

Se concluye que la desbridación triptica es un agregado valioso en las infecciones intrapleurales y en el hemotórax y que merece un uso más extenso. Los efectos colaterales son pocos y sin consecuencias. Su uso no está necesariamente contraindicado en presencia de fístula bronco-pleural.

#### RESUME

L'auteur présente certains cas où la trypsine peut être utilisée pour provoquer une action protéolytique. Ces cas comprenaient une pleurésie purulente tuberculeuse, une infection tuberculeuse de cavité extra-pleurale, une pleurésie purulente tuberculeuse avec germes associés, une complication pleurale infectieuse et non tuberculeuse survenue à la suite d'exérèse pour tuberculose, une pleurésie purulente post-opératoire non tuberculeuse, et un épanchement pleural bilatéral de nature indéterminée. Une guérison complète fut obtenue dans les deux cas de pleurésies purulentes tuberculeuses et dans les deux cas de pleurésie purulente post-opératoire, et une guérison presque complète dans le cas d'épanchement bilatéral d'origine indéterminée. Dans les trois autres cas, on put noter une amélioration caractérisée par la diminution de la viscosité du liquide, et sa stérilisation, ce qui contribua à de bons résultats chirurgicaux ultérieurs.

A la suite de cet essai encourageant, la trypsine fut utilisée successivement chez 22 autres malades, avec des résultats comparables. En outre des indications qui viennent d'être mentionnées, la méthode a été utilisée avec succès pour traiter des hémothorax post-opératoires ou traumatiques.

L'auteur conclut que l'action protéolytique de la trypsine est un auxiliaire de valeur dans le traitement des infections intrapleurales et des hémothorax, et que son usage devrait être plus étendu. Les complications de ce traitement sont minimales, et pratiquement négligeables. L'existence d'une fistule broncho-pleurale n'est pas une contre-indication formelle.

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# Topical Hydrocortisone in Pleuropericardial Exudations

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The anti-inflammatory and antiexudative properties of hydrocortisone, both systemic and topical, have been well established by numerous investigators. Similarly, it has been established that pharmacologically local hydrocortisone is far more active than cortisone.

On the basis of a report by Hollander et al.<sup>1</sup> of remarkable improvement with the use of hydrocortisone acetate in a case of pleural effusion complicating lupus erythematosus, we were induced to try the hormone locally in serositis complicating rheumatic fever. Favorable results were obtained, which were published in preliminary reports.<sup>2,3</sup> A fuller report was submitted to the International Congress of Rheumatic Diseases in Geneva, in 1953.<sup>4</sup>

## *Case Material*

Seven patients with unilateral or bilateral pleurisy and three with pleuropericarditis have been treated to date. All of the pleural complications were exudative, and for the most part of rheumatic origin. Seven of the 10 had previously been treated with cortisone acetate by intramuscular injection. The latter produced the usual general improvement but could not completely suppress the serosal effusion. Phenylbutazone in one had produced only partial improvement. Another had been treated for a few days with streptomycin and isoniazid, without success; the primary exudate had localized in both the pleurae and the pericardium. The 10th had pleural effusion following therapeutic pneumothorax for a circumscribed cavernous tuberculous lesion.

## *Technic*

Following partial drainage of the cavity, where necessary, from 75 to 100 mg of hydrocortisone acetate was introduced. Usually only one injection of hydrocortisone was given, in some cases, in which initial results were only partially successful, the injection was repeated once, and in rare instances twice, at six to eight-day intervals.

## *Laboratory Studies*

In addition to the clinical observations, the morphologic pattern of the cellular elements, as well as the relative viscosity<sup>5</sup> and mucoprotein content of the exudate<sup>6</sup> were studied. In addition, the following factors in the serum, in which the authors were particularly interested, were studied: total polysaccharides,<sup>7</sup> mucoproteins<sup>8</sup> and sedimentation rate (Westergren method).

From the Rheumatological Department of the Clinica Medica della Università di Milano, directed by Professor Luigi Villa.

### Results

The treatment produced a favorable effect in all of the patients. Exudation disappeared completely within one, two or three weeks, depending on the seriousness of the case.

Roentgenographic evidence of improvement in Case 3 is shown in figure 1. Treatment with topical hydrocortisone in the pleura was followed by reduction of exudate, in both the pleural and pericardial cavities. This effect was also observed in Case 5. The hormone is thought to reach the pericardial cavity either directly or by transmission via the lymphatic system.

In figure 2, the effect obtained by means of introduction of hydrocortisone acetate directly into the pericardial cavity is shown. In this patient, two further injections, into the pleural cavity, were later given. Therapy resulted in definite and lasting improvement.

Favorable results in a case of primary pleuropericardial serositis are depicted radiographically in figure 3. The initial injection into the pericardial space was followed by an injection into the pleural cavity. The patient was much improved within two weeks.

Unlike the response to intra-articular administration of hydrocortisone which produces marked changes in the synovial fluid, local instillation of hydrocortisone does not alter the physical or chemical characteristics of the pleural exudate but the mucoprotein composition. That is, there were no significant changes in morphology or viscosity (Table I).

### Discussion

Review of the case material presented indicates that local instillation of hydrocortisone acetate will reduce pleural exudation resulting from

TABLE I EFFECT OF TOPICAL HYDROCORTISONE ACETATE  
LABORATORY DATA OF THE PLEURAL EXUDATE AND OF THE SERUM  
OF CASE No 8

Date	Hydrocortisone acetate mg	Pleural Exudate			Mucoproteins		Serum		
		Differential Per Cent	Viscosity		Tyrosine mg Per Cent	Carbo- hydrate mg Per Cent	Total polysaccha- rides o d	Mucopro- teins mg Per Cent	Sedimen- tation rate (Katz Index)
April 10		neutrophils 11 lymphocytes 86 histiocytes 3	1 28		9 6	36	0 352	16 4	43
	50								
April 14		neutrophils 6 lymphocytes 93 histiocytes 1	1 17		8 2	29	0 340	15	44
April 22		neutrophils 7 lymphocytes 93	1 25		7 4	25	0 34	10 2	46
	100								
April 28		neutrophils 3 lymphocytes 97	1 30		7 2	19	0 315	11	17
May 9		neutrophils 8 lymphocytes 86 histiocytes 6	1 31		4 7	17 6	0 276	7	4
	100								



FIGURE 1 (Case No 3) Effect of local hydrocortisone acetate on pleural and pericardial effusion (A) Roentgenogram showing pleural and pericardial effusion before treatment, (B) 8 days after the introduction of 100 mg of hydrocortisone into the left pleural cavity, (C) 9 days after a second introduction of 75 mg of hydrocortisone, complete recovery

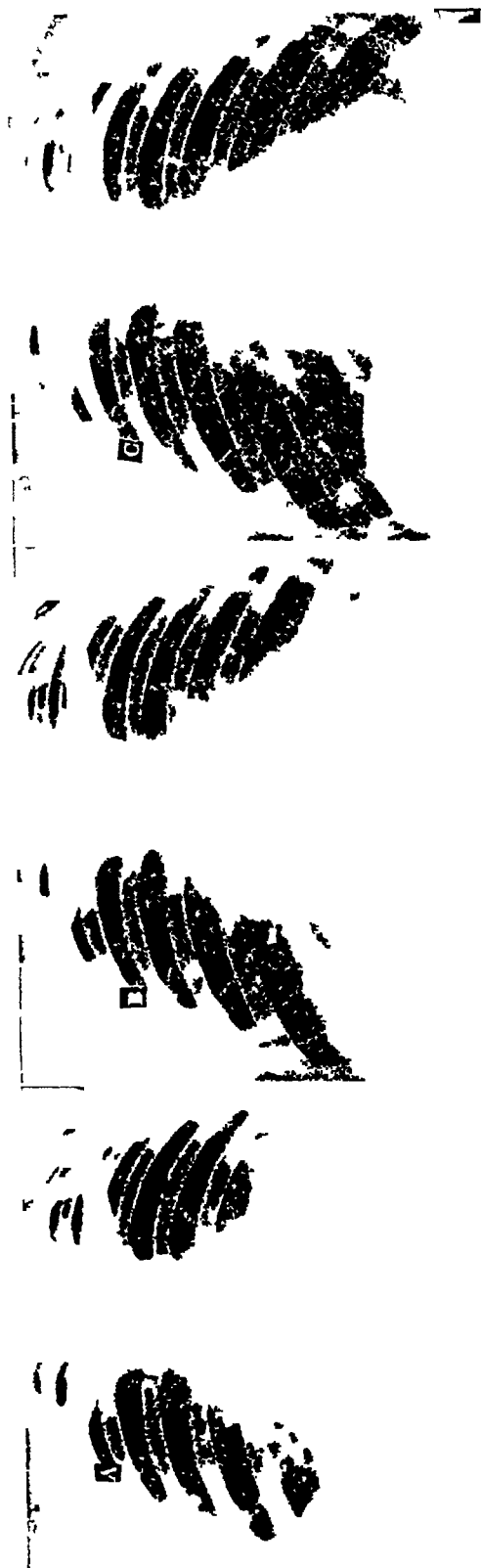


FIGURE 2 (Case No. 8) Effect of local hydrocortisone acetate on pleural and pericardial effusion (A) Roentgenogram showing pleural and pericardial effusion before treatment (B) 21 days after the introduction of 75 mg into the pericardial cavity and ten days after the introduction of 50 mg of hydrocortisone into the left pleural cavity (C) 13 days after a third introduction of 100 mg of hydrocortisone into the left pleural cavity complete recovery

rheumatic fever, even in cases in which systemic cortisone or hydrocortisone is unsuccessful. Two cases of possible tuberculous origin have some features in common with cases recently reported by Linquette et al,<sup>8</sup> who successfully treated tuberculous serositis with intramuscular cortisone and intrapleural instillation of hydrocortisone.

The use of hydrocortisone acetate as described in the present paper, minimizes the possible systemic effect<sup>9</sup> and reduces the likelihood of exacerbating the infectious process. Contraindications to pleural or pericardial instillation seem to be rare, even primary tuberculous lesions are not necessarily contraindications.

The precise way in which hydrocortisone affects the pleural effusion is not well understood. It has been suggested<sup>10, 11, 12</sup> that it may be a topical anti-inflammatory effect, and our results seem to confirm this.

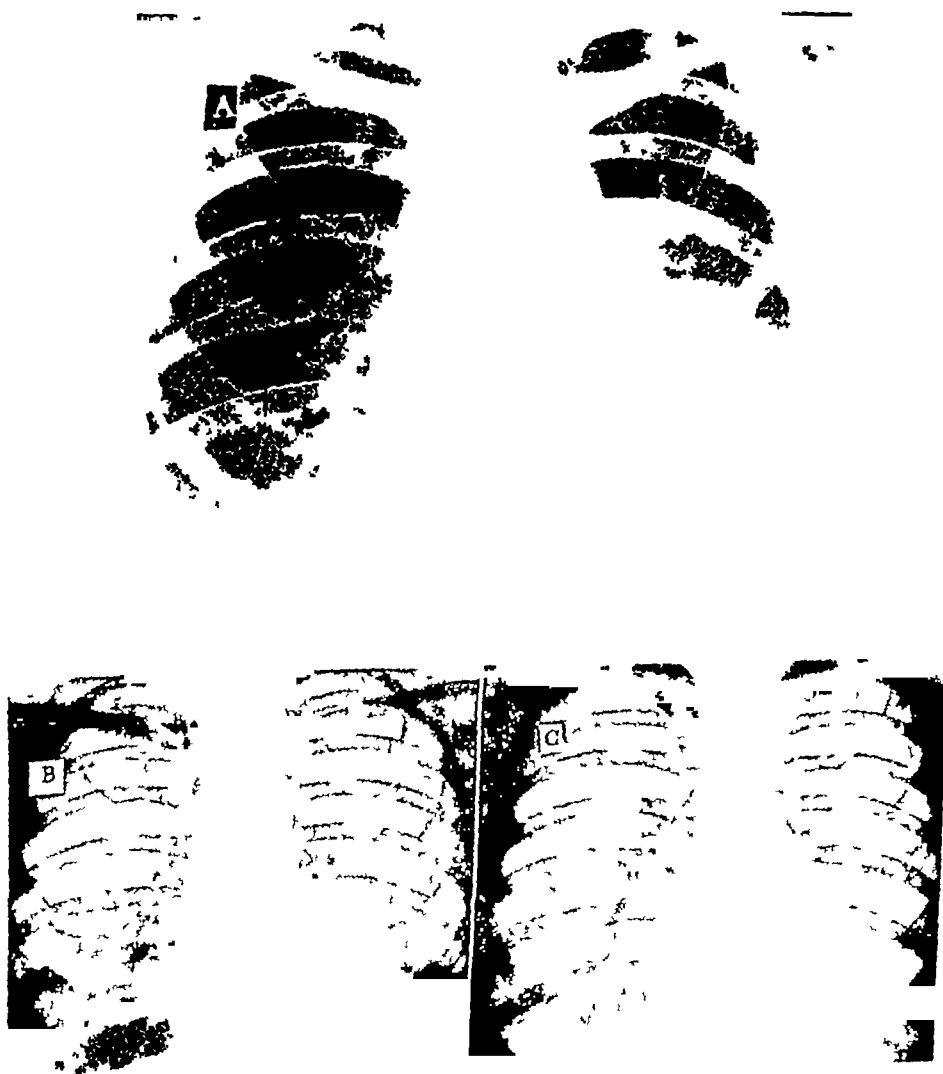


FIGURE 3 (Case No 9) Effect of local hydrocortisone acetate on pericardial and pleural effusions (A) Roentgenogram before treatment (B) 5 days after the introduction of 75 mg of hydrocortisone into the pericardial cavity (C) 8 days after a second introduction of 100 mg of hydrocortisone into the left pleural cavity complete recovery

## SUMMARY

Favorable results are reported with hydrocortisone acetate locally in 10 patients with pleural or pericardial changes accompanying rheumatic fever. These are ascribed to the anti-inflammatory properties of the drug. Contraindications to such therapy are rare.

## RESUMEN

Se refieren resultados favorables del empleo del acetato de dihidrocortisona localmente en 10 enfermos con alteraciones pleurales o pericárdicas que acompañaban a la fiebre reumática. Se atribuyen esos resultados a las propiedades anti-inflamatorias de la droga. Son raras las contraindicaciones de tal tratamiento.

## RESUME

Les auteurs rapportent des résultats favorables obtenus grâce à l'injection locale d'acétate d'hydrocortisone chez dix malades atteints de localisations pleurales ou péricardiques, au cours d'un rhumatisme articulaire aigu. Ces constatations s'expliquent par les propriétés anti-inflammatoires de ce produit. Ce traitement n'a que de rares contre-indications.

## ADDENDUM

Since this manuscript was prepared, we have treated 23 more cases of exudative effusions of different etiology in collaboration with Dr. F. Grassi of Vialba Sanatorium, with the following results: 1) topical hydrocortisone acetate may be used favorably in tuberculous pleurisy or in effusions of extrapleural pneumothorax, in these cases the use of antitubercular drugs and the valuation of lung lesions are mandatory; 2) forms of bacterial etiology may also be favorably treated, in association with antibiotics.

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# Heteroplastic Ossification in Chronic Lung Abscess\*

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Heteroplastic ossification is a condition characterized by the formation of true bone in soft tissues. The appearance of lamellae, canaliculi, and lacunae is prerequisite, bone marrow may be found. It is believed that pathologic calcification is a necessary precursor for ossification. A review of the entire subject is, therefore, warranted.

Pathologic calcification is usually found in diseased tissue, it is generally referred to as "dystrophic," as opposed to the "metastatic" type which accompanies metabolic disturbances, and which rarely undergoes ossification. Dystrophic calcification occurs most commonly in hyalinized fibrous tissues associated with chronic inflammation, such as in tuberculous scars, pericarditis and mitral stenosis.

While the exact mechanism of dystrophic calcification is not fully understood, certain factors relating to it have been established: there is an increased alkalinity of the tissues, a local increase of phosphatase and inorganic phosphates and antecedent fatty degeneration or necrosis<sup>1</sup>. Apparently local tissue injury and alkalization are both necessary, whether or not a toxic factor operates has not been established<sup>2</sup>. Meeker has demonstrated that the chemical composition of these calcified masses is the same as that of normal bone<sup>3</sup>.

Once dystrophic calcification has occurred, continuation of the process with resultant ossification is always possible. Karsner believes that the mechanism consists basically of the following sequence of events: calcification follows inflammation, granulation tissue then erodes this calcareous mass and new connective tissue cells from the granulation tissue undergo functional metaplasia and act as osteoblasts. Moore goes a step further, stating that the osteoblasts subsequently form trabecular bone, and between the trabeculae and spicules there is fibrous tissue or typical bone marrow<sup>4</sup>. Other than the presence of calcium salts, the exact stimulus to this metaplasia is not known. In many old deposits of calcium there may be gradual conversion to bone. It is probably similar to endochondral bone formation, with calcified masses taking the place of cartilage. Obviously, an adequate blood supply will favor ossification. Wells states that, "in order to have ossification of calcific deposits, certain conditions of relationship between calcium salts, fibrous tissues and blood supply evidently must be exactly met<sup>5</sup>". Herbut points out the "vicious cycle" aspect of heteroplastic ossification: the presence of bone in an abscess prolongs the infection which in turn favors bone formation<sup>6</sup>.

Grossly, ossification in soft tissues can not be differentiated from calcification. Microscopically, the elements of bone are irregularly arranged.

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When marrow is present it is usually fatty, chronic inflammation surrounds the bone. Cartilage has not been observed in man.<sup>2</sup>

Ossification in chronic pulmonary lesions is said to be fairly common, especially in bronchial cartilages and in tuberculous scars. Wells and Dunlap<sup>7</sup> collected 53 cases of diffuse ossification of lungs unassociated with tuberculous scars occurring in aged men and young individuals with mitral stenosis. Characteristically, small flakes of bone were found throughout the lungs.

Despite the fact that the textbooks state that ossification can occur in chronic pulmonary infections, there is a paucity of such cases in the literature. No report can be found in which *true* bone formation occurred in a lung abscess. We present such a case.

### *Case Report*

A 35 year old white female was admitted to the Southern Division of the Albert Einstein Medical Center in January, 1951, with the history of chronic cough accompanied by copious expectoration of muco-purulent material. About one year previously she had been hospitalized because of fulminating Friedländer's pneumonia. The present complaints had persisted since recovery from the acute episode. X-ray films showed cavitation in the left upper lobe (*Figs 1 & 2*). Frequent bronchoscopies consistently revealed purulent discharge from the left upper lobe bronchus. Cultures had shown a mixed infection. Antibiotics offered no improvement. Consequently, left upper lobectomy was performed. Dense adhesions necessitated extrapleural dissection. Palpation of the abscess wall elicited a denseness that suggested calcification. In fact, there were extensions of calcified material from the left upper lobe to the anterior mediastinum and posterior chest wall.

Examination of the specimen revealed a large abscess cavity measuring 8 x 6 x 4 cms. A large portion of the wall was calcified, the remainder was composed of thick fibrous tissue. The main stem bronchus led into the cavity (*Fig 3*). Microscopic sections of abscess wall revealed fibrous tissue in which there appeared new alveolar formations and marked chronic inflammatory cell infiltration. Portions of bronchus were markedly dilated and contained areas of bone and bone marrow metaplasia. The surrounding lung parenchyma gave evidence of severe chronic bronchitis, bronchiolitis and associated bronchiectasis (*Fig 4*).

The immediate post-operative course was satisfactory. She is now enjoying good health, four years following surgery.

### *Discussion*

In this case, a chronic lung abscess developed following recovery from acute Friedländer's pneumonia. Fortunately, only about 1 per cent of all bacterial pneumonias are caused by Friedländer bacilli. Prior to the antibiotic era, the mortality from such infections was 50-80 per cent.<sup>8</sup> Today, however, most persons with these acute pneumonias recover, we shall therefore, no doubt, see a higher incidence of chronic pulmonary disease secondary to Friedländer infections. One may further speculate that there will appear more instances of heteroplastic ossification, since apparently all the factors favoring this phenomenon will be present: tissue necrosis, chronic inflammation with fibrosis and a rich blood supply.

### SUMMARY

A case is reported of chronic lung abscess due to Friedländer infection in which there occurred heteroplastic ossification.

The presence of *true* bone was accompanied by actual *bone marrow* formation.





FIGURE 1

FIGURE 2

*Figure 1* X-ray film of Chest. Cavity in left upper lobe.—*Figure 2* Bronchogram  
Bronchus leads into cavity in left upper lobe.—*Figure 3* X-ray film of resected Lobe  
Calcification is demonstrated in the wall of the cavity



FIGURE 3

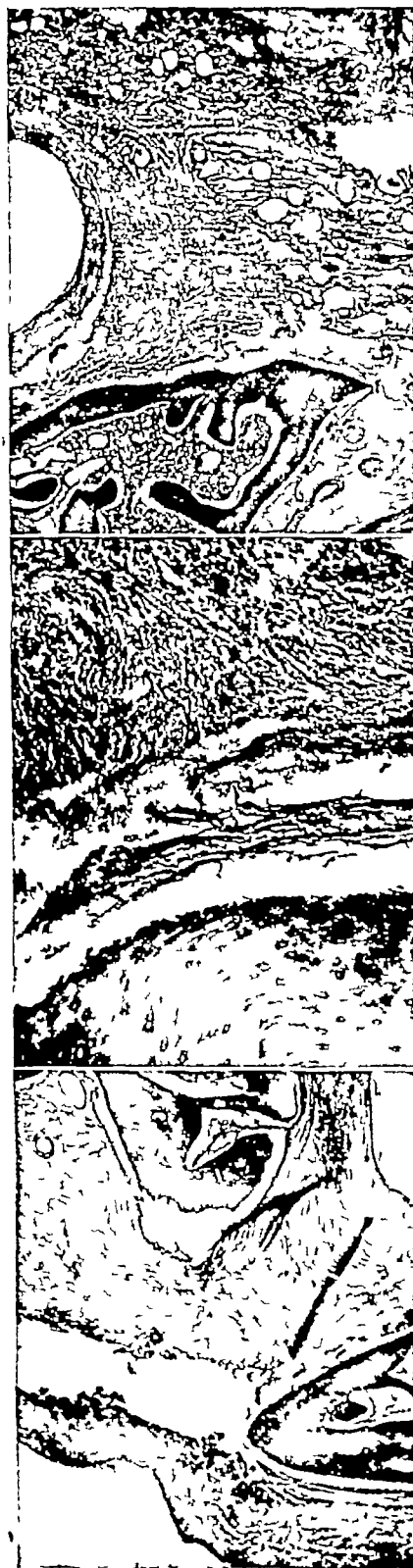


FIGURE 4A

FIGURE 4B

FIGURE 4C

Photomicrographs *Figure 4A*—20X Low power cancellous lamellar bone with surrounding inflammatory fibrous reaction in lung tissue *Figure 4B*—100X High power of A *Figure 4C*—20X Low power Bone with marrow elements evidencing true ossification

As far as can be determined this is the first such case reported in the literature of solitary pathologic ossification in a chronic lung abscess

The mechanism of pathologic calcification and ossification is reviewed

#### RESUMEN

Se relata un caso de absceso pulmonar crónico, debido a infección por bacilo de Friedlaender en el que ocurrió osificación heteroplástica

La presencia de *verdadero hueso* se acompañó por formación de *médula ósea*

Hasta donde puede saberse, este es el primer caso referido de esta índole de osificación solitaria patológica en un absceso pulmonar crónico

Se revisa el mecanismo de la calcificación patológica

#### RESUME

Les auteurs rapportent une observation d'abcès chronique du poumon à bacilles de Friedlander, dans laquelle se constituait une ossification hétéroplastique

La présence d'os véritable s'accompagnait de formation de moelle osseuse en activité

Les auteurs pensent qu'il s'agit du premier cas rapporté dans la littérature, ayant donné lieu à une telle ossification isolée, pathologique, au cours d'un abcès chronique du poumon. Les auteurs passent en revue le mécanisme des calcifications et des ossifications pathologiques

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# Contra-Lateral Spontaneous Pneumothorax as a Complication of Intrathoracic Operations<sup>\*</sup>

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There is a definite trend of reduced mortality and morbidity following thoracic surgical procedures. This is due largely to prevention as well as recognition and prompt treatment of postoperative complications. One of the unusual complications which does occur from time to time is contra-lateral spontaneous pneumothorax. Such a complication following collapse therapy for pulmonary tuberculosis has been repeatedly observed,<sup>1</sup> however, this occurrence following intrathoracic operations is apparently rare. The exact incidence is difficult to determine since it is doubtful if all recognized cases have been reported and, also, it is possible that not all such complication has been recognized. The latter possibility is quite great in view of the nature of spontaneous pneumothorax, since, at post mortem, the pathologist may be misled in his conclusions without an antemortem suspected diagnosis.

So far, there have been eight cases of this type reported in the literature, Stephen's<sup>2</sup> three cases reported in 1936 being the earliest available description of such an incidence. More recent references in the literature are case reports of Gleason and Kent<sup>3</sup> in 1949 (one case), Melick and Gutekunst<sup>4</sup> in 1950 (one case), Beno and Weisel<sup>5</sup> in 1952 (three cases). Out of these eight cases so far reported, five survived and three died as the direct result of this complication. Death in each instance was apparently due to delay in recognition and treatment. This report is being made in order to re-emphasize the potential danger and outline the treatment which, if promptly instituted, can alter the course of this otherwise fatal complication.

## *Report of Cases*

*Case 1* J. G., East Orange General Hospital No. 83120, a 13-year-old white male was admitted on November 4, 1950, with symptoms of shortness of breath and cyanosis of 24 hours duration. Diagnosis at the time of admission was spontaneous left pneumothorax.

Family history and personal history were negative except for measles at the age of five and virus pneumonia when seven years old.

History of the present illness dated to about three months prior to this admission when he had a similar episode of spontaneous pneumothorax on the left side which subsided after a few days of bed rest. Two months later, another attack occurred on the left side and again responded to a few days of bed rest.

Physical examination was negative except for a moderate amount of cyanosis and presence of pneumothorax on the left side. Chest roentgenogram (Fig. 1) revealed 75 per cent collapse of the left lung. Over the apex of the left upper lobe, a large cystic area could be outlined. The right lung seemed to be normal.

Laboratory studies were within normal limits. He was treated initially with bed rest and removal of 3 liters of air from the pleural cavity.

Since this was the third episode of spontaneous pneumothorax within a relatively short time, and the chest roentgenograms showed the presence of a cystic area over the apex of the left upper lobe, resection of the cyst was decided upon and carried out on the seventh day after admission.

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FIGURE 3

FIGURE 2

FIGURE 1

Through a postero-lateral incision, the pleural cavity was entered and a giant cyst of the left upper lobe was found, with three small satellite cysts. The large cyst was held out by fine adhesions from the posterior aspect of the pleural cavity, the site of rupture could not be seen even after submersion of the lung in saline solution. The cyst was resected and the stump closed by a continuous suture. The lung was re-expanded and the chest closed. Pathological examination of the specimen revealed it to be a cyst with alveolar cell type of epithelial lining.

Postoperative condition of the patient was extremely smooth. In fact, he was ambulatory on the second postoperative day. On the third postoperative day, while getting up from the bed, he experienced a sudden sharp pain over the right side of the chest and became extremely cyanotic. Physical examination revealed the presence of pneumothorax on the right side. Immediately, a needle was inserted in the right pleural cavity (contra-lateral to the operative side) and high positive pressure reading obtained. Four thousand cubic centimeters of air were removed. The patient's condition improved enough to allow a chest x-ray film (Fig 2). This revealed 90 per cent collapse of the right lung and an area over the apex of the right upper lobe suggestive of a cyst. Conservative therapy by means of repeated needle aspirations led to only a temporary relief of dyspnea. It was obvious that something other than repeated chest aspirations would be necessary in order to overcome the recurring tension-pneumothorax. Eight hours after the onset of the contra-lateral spontaneous pneumothorax, under local anesthesia, a thoracoscope was introduced through the fifth interspace and midaxillary line. Exploration revealed the presence of a collapsed lung, over the apex of the upper lobe, a giant cyst was seen held to the parietal pleura by multiple fine bands of adhesion. The area of the tear could not be visualized. A catheter (No 12 French) was inserted in the pleural cavity and connected to a Steadman pump. The suction apparatus was arranged with a water trap and suction maintained at 15 centimeters of water. This was soon found to be inadequate because of continuous leakage of a large amount of air for eight days with no roentgenological sign of improvement in the state of the collapsed right lung. It was then assumed that probably the intrapleural adhesions prevented spontaneous closure of the ruptured area and that the air was leaking into the pleural space as fast as it was being removed. Consequently, right thoracotomy was performed on the ninth day after the original operation on the left side. The right lung seemed to be completely collapsed. A giant cyst was found over the right upper lobe, quite identical to the one removed from the left side. There were several fine adhesions between the cyst and the chest wall. The site of rupture was 3.5 centimeters in length. The cyst was removed and the stump closed with interrupted suture and the lung expanded. His general condition following this second operation was satisfactory and the postoperative course uneventful. He was ambulatory on the second and discharged home on the ninth postoperative day.

The follow-up roentgenogram of the chest showed satisfactory re-expansion of both lungs (Fig 3). Examination one-and-one-half years following bilateral thoracotomy revealed good physical condition. There has not been re-occurrence of spontaneous pneumothorax.

**Case 2** S.M., Mountainside Hospital No 95396, a 46-year-old Negro male was admitted on June 9, 1952, with chief complaint of shortness of breath on moderate exercise. History of present illness dated to about a year ago when he experienced an attack characterized by sharp pain in the right chest. He was then hospitalized at Morristown Memorial Hospital where a diagnosis of spontaneous pneumothorax was made. He was treated by bed rest and discharged after a few days to continue bed rest at home. While at rest, he experienced several similar attacks of dyspnea, however, he gradually improved and for the last three months felt well except for persistent respiratory embarrassment when walking or climbing stairs. About a month before this admission, a roentgenogram of the chest revealed pneumothorax still present, the lung 50 per cent collapsed and a fluid-containing cyst over the right upper lobe. He was then referred to The Mountainside Hospital for observation and treatment. Previous general health had been good. The family history was negative.

The initial physical examination disclosed a well-developed, well-nourished Negro in no acute distress. Temperature, pulse and respirations were normal. The chest showed good expansion on the left side but none on the right. Breath sounds were absent on the right side. No rales or rhonchi were heard on the left.

The initial laboratory findings were negative except for the presence of moderate hemoconcentration (Hematocrit 52 volume packed red blood cells per 100 cubic centimeters of blood), sputa and gastric washings were negative for tuberculous bacilli. Roentgenograms of the chest revealed the right lung about 50 per cent collapsed by pneumothorax with a large area of radiolucency over the apex, suspected to be a cyst (Fig 4).

A needle was introduced in the pneumothorax space and a negative reading obtained (-14, -11). Bronchoscopic examination failed to reveal the presence of endobronchial pathology.

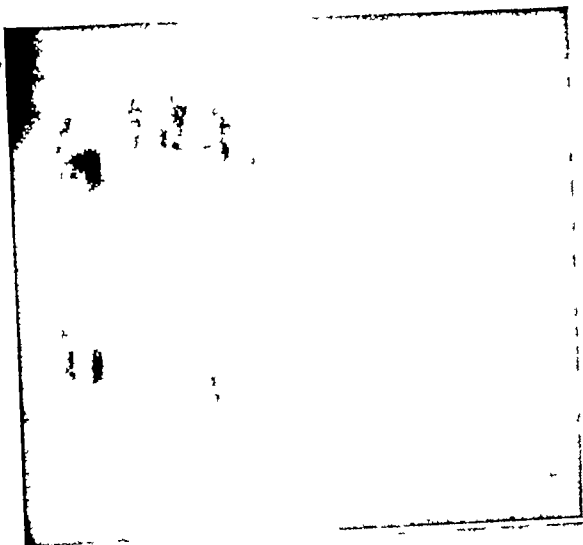


FIGURE 6



FIGURE 5



FIGURE 4

On June 16, 1952, thoracotomy was performed on the right side through a postero-lateral approach. Exploration of the right lung revealed the presence of a single large thin-walled emphysematous bulla of the right upper lobe. The lung was held down by a pleural membrane. Some pleural fluid was present. The cyst was opened widely and resected by keeping tension on the cyst wall. Thus, an accurate identification of the attachment of the base of the cyst to the lung was made and the stump closed with interrupted fine silk. Decortication of the lung was performed following the standard technique, drainage tubes inserted and the chest closed in routine manner.

Postoperative condition was satisfactory. Portable roentgenogram of the chest made the following morning revealed complete re-expansion of the lung on the operative side. However, at 8 A.M. of the same day (28 hours postoperative), he suddenly became dyspneic. Physical examination revealed the trachea to be deviated to the operative side. No breath sound could be heard over the left chest. Immediately, a needle was inserted in the pleural cavity and 2000 cubic centimeters of air removed. Following the above procedure, his condition improved enough to allow a bed side roentgenogram of the chest which substantiated the clinical impression of contra-lateral spontaneous pneumothorax (Fig 5). Since the improvement was temporary, two hours later, under local anesthesia, a catheter was introduced through the third anterior interspace and midaxillary line into the left pleural cavity and connected to the underwater drainage bottle. Dramatic improvement occurred following the above procedure. About 24 hours later his condition again deteriorated. Respirations became labored and pulse thready. Examination revealed the reason for this re-occurrence to be clogging of the drainage tube. This was corrected and his condition improved. On the fourth postoperative day, he experienced a sudden sharp pain over the left chest and within the space of one hour, a large amount of subcutaneous emphysema over the head and neck was noticed, while the drainage tube was apparently in good working condition. He became extremely cyanotic and blood pressure and pulse became unobtainable. Through an anterior-intercostal approach, the left chest was immediately opened and a large amount of air under pressure escaped from the pleural cavity. The heart was found at standstill, cardiac massage was instituted and after about two minutes, cardiac function was restored. The blood pressure came back to normal. Exploration of the left lung at this time revealed the presence of a giant cyst over the left upper lobe. The line of rupture measured about 5 centimeters in length. The latter was kept patent by several intrapleural adhesions. The cyst was excised and the stump closed with fine silk. Two large drainage tubes were inserted in the pleural cavity and the chest closed in routine manner.

After this episode, the postoperative course was entirely uneventful and he was discharged home on his 12th postoperative day.

Pathological diagnosis of the cyst removed from the right, as well as from the left upper lobe, was giant emphysematous bulla.

The follow-up roentgenogram of the chest showed satisfactory re-expansion of both lungs (Fig 6). Examination six months following bilateral thoracotomy revealed no symptom and he was working full time as a laborer. There has not been re-occurrence of spontaneous pneumothorax.

### *Discussion*

Several mechanisms have been proposed with regard to production of spontaneous contra-lateral pneumothorax. Stephens<sup>2</sup> stated that the etiologic factor in each of his three cases was a communication through the mediastinal wall, although the site of tear could not be visualized at necropsy. This view was also shared by Kneopp.<sup>6</sup> However, in the case reported by Gleason and Kent, and three cases reported by Beno and Weisel, a ruptured emphysematous bleb was believed to be the main factor in the production of this complication. In the two cases presented here, a ruptured emphysematous bleb was found to be the only reason for the production of the spontaneous contra-lateral pneumothorax. In both cases, the site of rupture was well demonstrated at the time of exploration.

Symptoms and physical findings are those of a spontaneous pneumothorax, the degree of respiratory embarrassment however, seems to depend on the amount of tension present in the pneumothorax space as well as on the degree of fixation of the mediastinum. The case described by



Gleason and Kent in which left lower lobectomy for bronchiectasis had been performed, dyspnea and cyanosis were only moderate while in the two cases just described, where pulmonary pathology was not of inflammatory nature, the respiratory embarrassment was severe.

In analyzing the eight cases reported in the literature, it is striking that death in each instance was due to delay in recognition and institution of treatment of this condition. Treatment should be carried out on the basis of physical findings alone, if the condition of the patient does not allow time to lose to have roentgenograms of the chest. Emergency treatment is simple and effective. Decompression of the tension pneumothorax by immediate thoracentesis is all that is needed. Roentgenological examination and other diagnostic procedures should be done only after the severe subjective symptoms are relieved. Alexander<sup>7</sup> stated, any diagnostic measure which is not capable of relieving the respiratory embarrassment is contra-indicated.

After the acute episode is overcome, intrapleural catheter drainage and continuous suction should be applied. Thoracotomy may become necessary in instances such as in the case of Gleason and Kent and the two cases here presented.

#### SUMMARY

1 Two cases of spontaneous contra-lateral pneumothorax following resection of pulmonary cyst are reported.

2 In both cases, ruptured contra-lateral emphysematous bleb was proved to be the etiologic factor.

3 The dangers of contra-lateral spontaneous pneumothorax following intrathoracic operations are that of tension pneumothorax, collapse of the lung opposite to the operative side and mediastinal shift. The severity of respiratory embarrassment resulting from the above depends on the degree of fixation of the mediastinum. If the latter is freely mobile, the respiratory embarrassment may quickly be followed by complete failure.

4 The diagnosis is made on the basis of physical findings of pneumothorax opposite the operative side in a patient presenting an acute respiratory distress.

5 Emergency treatment should be undertaken without delay since the time lost until chest roentgenogram is taken may precipitate irreversible respiratory failure. Treatment is simple and effective. The decompression of the tension pneumothorax by immediate thoracentesis is all that is needed. Roentgenological examination and other diagnostic procedures should be done only after the severe respiratory symptoms have been relieved.

#### RESUMEN

1 Se refieren dos casos de neumotórax espontáneo contralateral, después de la resección que ampollas pulmonares.

2 En ambos casos, se demostró que la causa fué la ruptura de ámpuas enfisematosas contralaterales.

3 Los peligros del neumotórax espontáneo contralateral, consisten en que puede ocurrir el neumotórax a tensión, colapso del pulmón opuesto al que se opera y desplazamiento del mediastino. La severidad del trastorno respiratorio que resulta de lo anterior, depende del grado de fijación del mediastino. Si éste es libremente móvil, el trastorno respiratorio puede ser sucedido de insuficiencia completa.

4 El diagnóstico se hace sobre los hallazgos físicos de neumotórax opuesto al lado que se opera en un enfermo que tiene grandes trastornos respiratorios.

5 El tratamiento es sencillo y eficaz. La descompresión del neumotórax a tensión, es todo lo que se requiere. El examen radiológico y otros procedimientos de diagnóstico deben intentarse solo cuando los síntomas severos se hayan aliviado.

#### RESUME

1) Les auteurs rapportent deux cas de pneumothorax spontané controlatéral faisant suite à la résection d'un kyste pulmonaire.

2) Dans les deux cas, on put démontrer que la rupture d'une bulle emphysémateuse controlatérale en avait été responsable.

3) Les dangers du pneumothorax spontané controlatéral faisant suite aux interventions intrathoraciques sont fonction de la pression intrapleurale du pneumothorax, de l'importance du collapsus du poumon et de la déviation médiastinale. La gravité de la gêne respiratoire qui en résulte dépend du degré de fixité du médiastin. Si celui-ci est complètement libre, la gêne respiratoire peut être suivie rapidement d'une insuffisance respiratoire complète.

4) Chez un malade présentant une gêne respiratoire aiguë, le diagnostic de pneumothorax du côté opposé au poumon opéré se base sur les constatations physiques.

5) Le traitement doit être entrepris d'urgence. Le temps que l'on perdrait à attendre les résultats de la radiographie pourrait amener au stade d'insuffisance respiratoire irréversible. Le traitement est simple et efficace. La suppression de l'hyperpression gazeuse intrapleurale par simple thoracocentèse est suffisante. Ce n'est qu'après la disparition des signes graves d'insuffisance respiratoire qu'on pourra faire appel à l'examen radiologique et aux différents autres procédés de diagnostic.

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# Unexpected Death in Asthma

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The prognosis in asthma, so far as duration of life is concerned, is generally considered to be good and it is a fact that the majority of asthmatic patients, although they may have to live a restricted life, learn to compensate for their disability and may even accomplish a great amount of useful work. In the usual course of events emphysema is likely to supervene, and death most commonly occurs from congestive heart failure or from respiratory infection. It is customary to console the asthmatic patient with the assurance that the duration of life is not likely to be affected, and this optimistic view is commonly justified in the event.

A study of the text books on general medicine shows that authors are almost unanimous in supporting the opinion that asthma by itself is not a lethal condition, and reassuring views are expressed on prognosis. Osler and McCrae (1921) quote the assertion of Oliver Wendell Holmes that asthma is "the slight ailment that promotes longevity." Monro (1924) considers that the prognosis is good, if the cause can be removed, the liability to asthma is not inconsistent with many years of fitness for work. Conybeare (1936) states that it is doubtful whether death has ever been caused by uncomplicated asthma.

Most authors of text books on disease of the respiratory tract are, however, more cautious. Davidson (1948) considers that the outlook in asthma is very uncertain, but that the actual attacks are "very seldom" fatal. Coope (1948) quotes the statement that no one ever dies from an asthmatic attack and comments that this is not entirely true, but he goes on to suggest that sudden death occurs as a result of established cardio-respiratory changes. Cecil and Loeb (1951) divide their asthmatic cases into two groups, "extrinsic" and "intrinsic." The extrinsic cases are those which occur in young people; the intrinsic group includes patients in whom the asthma begins after the age of 30, and the factors concerned are stated to be bacterial, allergy, depletion, infection, psychic causes, polypoid sinusitis, emphysema and foreign bodies. In this intrinsic group they state that the mortality is 7.6 per cent but they do not refer to sudden death and it would appear that most of their fatal cases occur as a result of organic disease. Norris and Landis (1940) state that, "contrary to the older writers, death does not result from uncomplicated bronchial asthma," and they take the view that congestive heart failure or acute respiratory infection are the usual causes of death, although they mention the possibility of obstructive atelectasis. It does not appear, however, from their description that they recognize the sudden type of death which is discussed in this paper.

Recent studies of fatal asthma have been published by Williams (1953) and by Earle (1953). Williams quotes the Registrar General's figures of deaths from asthma and he presents records of 181 cases of death from status asthmaticus. He suggests that death from this cause occurs predominantly in patients over the age of 30 years and concludes that infection plays a dominant part in the etiology of death from status asthmaticus. Earle finds that "death from uncomplicated bronchial asthma is not so rare as was once supposed. Death usually results from asphyxia produced by excessive mucous secretion blocking the air passages, whereas bronchospasm plays a minor role." He draws attention to the dangers of morphine and aspirin in sensitive subjects. He goes on to state that "some asthmatics die suddenly without sufficient cause being demonstrated at necropsy, vagal inhibition of the heart by physical or psychological stimuli is a possible mechanism." Houston et al (1953) record a series of nine cases of fatal status asthmaticus, carefully studied at necropsy, from which they conclude that loss of the ciliated bronchial epithelium seems the most probable explanation for the formation of mucus and bronchial obstruction.

Occurrence of a fatal result in status asthmaticus does not come as a surprise or shock to the relatives or to the doctor, because the patient is gravely and increasingly ill over a period of hours or days. During the past few years, however, it has become apparent to the writer that there is a small number of asthmatic patients who die quite suddenly in an attack which does not differ in any respect from the attacks of asthma to which these patients are accustomed. This condition is completely different from that which is termed status asthmaticus. Rubin (1947) describes one such case in which autopsy revealed over-distention of the lungs, with the heart in systole. He also quotes L. Unger who reported an analogous instance in which the findings were very similar. The purpose of this paper is to describe the clinical findings in a series of nine cases of asthma in which sudden death occurred without any satisfactory explanation. It is essential to realize the possibility of such an event, for unexpected death in what appears to be a perfectly innocent condition is liable to come as a great shock to the relatives, particularly if they have been assured that asthma is not a fatal complaint. From the scientific point of view it is necessary for the fact to be placed on record that spasmodic asthma, in itself, is a possible cause of death. Unless this fact is recognized, the medical attendant may be tempted to postulate some additional condition which is known to cause sudden death, such as coronary thrombosis, in order to explain the occurrence but there is no evidence which would suggest that asthmatic subjects are prone to develop coronary disease and the mode of death in patients described here did not suggest coronary thrombosis or, in fact, sudden heart failure. The clinical picture in each case was that of sudden failure of respiration, for which no plausible explanation can be advanced.

The present series consists of a group of nine cases which have been under observation and treatment during the past 10 years. In order to

save space the clinical details are presented in the form of a table and the various factors are considered under the headings suggested by the present writer in a previous paper (1936)

FACTORS CONCERNED IN ASTHMA (9 cases)

Case No	Sex	Age of Onset	Age at Death	Total duration of illness	Family History of Asthma	Skin Tests	Upper respiratory tract disease	Broncho-pulmonary changes	Psychological factors	Evidence of heart strain
1	F	51	51	6 mths	+	0	0	0	+	0
2	F	54	55	10 mths	0	0	0	0	+	Hypertension
3	F	42	44	2 yrs	+	0	+	0	+	0
4	F	57	59	2 yrs	0	+	0	0	+	Enlarged Heart
5	F	37	42	5 yrs	0	0	+	+	+	0
6	M	57	67	10 yrs	0	0	0	0	+	Hypotension
7	M	47	48	10 mths	0	0	+	0	+	0
8	M	64	66	2 yrs	0	0	+	0	+	0
9	M	47	47	5 mths	0	0	+	0	+	0

Consideration of this group of cases shows some common factors which may be significant. In the first place the age of onset was confined to patients over the age of 35 years, and it is noteworthy that no less than six died suddenly within two years of the onset of asthma. There was little evidence of an allergic factor, the upper respiratory tract was significantly diseased in six. Careful examination revealed organic change in the lungs in only one.

The heart was examined clinically, radiologically and by the electrocardiogram in each case. Only once was any enlargement found, in a woman aged 57 years, in one there was hypertension and in another the blood pressure was decidedly low (90/55). In none of these cases, however, could there be any suggestion of heart strain leading to sudden death and the state of the circulation was about the same as one would expect to find in any similar group of adults. The most significant feature, shown by the table, is that a distinct "psychological" factor was considered to be present in every case, it is necessary, of course, to be very careful in assessing the significance of a psychological factor in any asthmatic patient unless a full investigation has been carried out in order to determine which other factors are present. In a previous paper (1936) it was considered that there was a significant psychological factor in 74 of a series of 150 cases, so that the presence of a psychological factor in each of these nine patients may be regarded as being noteworthy. In fact, an interesting point emerges from a review of this group. If one considers a large group of asthmatic patients the most striking feature as a rule is the cheerfulness with which the patient faces up to his disability. In the majority of cases the patient makes light of the moderate attack of asthma and carries on with his work in a way which might seem inexplicable to a non-asthmatic person. Each of these nine patients reacted quite differently. In all there was a defeatist attitude almost from the start, and in seven the patients expressed a conviction of impending death. It seems

to be almost certain that this unusual attitude is significant, and it makes one wonder whether as yet we fully understand the mechanism by which life ceases. In four of the cases described here death occurred in the presence of a qualified observer. In each case the event was sudden and completely unexpected, within a few minutes of the onset of what appeared to be an average attack of asthma, and the only apparent explanation in each instance was a sudden failure of respiration. It may also be significant that eight of these patients died at home, and it is possible that the feeling of security conveyed by a hospital and an ever-present nursing staff is an important factor in guarding the patient against an event of this sort. The prevalent feeling in every case was a complete loss of confidence in the future and an entirely hopeless attitude towards life. Consideration of the observations presented here leads to the conclusion that an asthmatic patient who exhibits a pessimistic attitude should be regarded with some suspicion, and the prognosis in such cases should be carefully framed in order to forewarn the relatives that sudden death is a possibility.

It is difficult to see what measures can be taken to support this particular type of patient. Naturally all the usual methods of treatment will be given in the ordinary way, but the results of standard treatment in this series were unsatisfactory. In some ways there is a resemblance to a depressive psychosis, and it might be worth while considering some such treatment as electro-convulsant therapy in the depressed asthmatic. The treatment of the acute emergency depends upon the adoption of instant measures and it is unlikely, therefore, that the opportunity for immediate therapy will often arise. It does not appear that adrenalin is of the slightest value but, if available, the most suitable method from the pharmacological point of view would be the injection of 5 to 7 mls of nikethamide into a vein.

The fact that sudden death may occur as a result of asthma may have some medico-legal importance and, in this connection, one of the cases in this group may be described in some detail. He was an ex-regular army officer aged 47 years. Nasal polyps were removed in 1936, after which there was persistent nasal catarrh, with further operations in 1942 and 1945. In May 1949, he experienced a sudden severe attack of asthma which responded to treatment with adrenalin, but the condition recurred in July and he was admitted to hospital. The asthma recurred at intervals for no apparent reason. The hospital note stated that "although the general condition is satisfactory, the patient has no confidence in himself." It was considered that the psychological state was an important factor in failure of the patient to respond to treatment. He was discharged on 27th September 1949 and he died quite suddenly at home on 1st October 1949. In this case a point of special importance arose. The death certificate stated that the cause of death was "coronary thrombosis" and "status asthmaticus," although the clinical features of both conditions would appear to have been absent. There was no qualified observer present at the moment of death and it is therefore impossible to be quite

sue whether the patient did in fact die from coronary thrombosis, but a consideration of the clinical circumstances does not show any reason to suspect the presence of heart disease, and it appears much more likely that he died from asthma. A claim put forward to the Ministry of Pensions on behalf of his widow was rejected on the ground that coronary occlusion does not bear any relation to asthma and that therefore the cause of death could not in any way be attributed to War Service. In this case there had been a severe degree of nervous strain which preceded the actual development of asthma, and it is probable that this was the most important factor in producing the fatal result. It is open to argument whether the asthma was due to War Service, but the suggestion of coronary thrombosis furnished an effective red herring which obscured the true issues in this case.

#### SUMMARY

Death may occur quite suddenly in an attack of asthma. Patients who appear to be liable to this disaster are those who develop asthma after the age of 35 years and, in particular, those who exhibit a depressive tendency. When present this tendency should be treated. It is suggested that, in propitious circumstances, an emergency might be met by the intravenous injection of 5 to 7 mls of nikethamide.

#### RESUMEN

Puede ocurrir la muerte repentina durante un ataque de asma. Son más capaces de sufrir esto, aquéllos enfermos en los que aparece el asma después de los 35 años y en especial aquéllos que muestran una tendencia depresiva. Cuando esta tendencia se presenta, debe combatirse. Se sugiere que en circunstancias propicias se puede hacer frente a esta emergencia por la inyección intravenosa de 5 a 7 miligrs de niketamida.

#### RESUME

On peut voir survenir la mort presque subite au cours d'une crise d'asthme. Les malades qui semblent susceptibles d'une telle évolution sont ceux dont l'asthme se constitue après 35 ans, et en particulier ceux qui ont une tendance dépressive. Quand on constate cette tendance, on doit lui opposer une thérapeutique. L'auteur conseille que dans certaines circonstances, il puisse être nécessaire de faire d'urgence une injection intraveineuse de "nikethamide".

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## Case Report Section

### Selective Pneumothorax A Complication of Bronchoscopy\*

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The occurrence of pneumothorax with mediastinal and, or, subcutaneous emphysema is an infrequent complication of bronchoscopic examination<sup>1, 2, 4, 6</sup> The site of rupture of the trachea or main bronchi has been obvious in some, but in others, no cause for this complication has been determined

The visualization of selective pneumothorax without emphysema as a complication of bronchoscopy has not been previously reported

#### CASE REPORT

R F (R No 3341), a 63 year old Negro male, had shortness of breath and pain in the right chest of two years duration Symptoms had been intermittent One year previously he had a small hemoptysis X-ray film of the chest at that time was reported as negative Two months previous to present admission he had spit up several teaspoonfuls of bright red blood The chest x-ray film, at that time, was reported as showing an infiltration of the right upper lobe He (Fig 1) was bronchoscoped and no lesion was found, but he was referred for hospitalization

X-ray film of the chest (Fig 2) on admission to this hospital revealed pneumothorax selectively collapsing the right upper lobe He had no symptom referable to pneumothorax He was rebronchoscoped and again no abnormality was found

He was explored and on finding a mass in the right upper lobe, pneumonectomy was performed The surgical specimen revealed a fairly well demarcated, hard, light grey mass arising from the posterior and anterior branches of the right upper lobe bronchus The mass extended from the point of origin for a distance of 2 cm along the course of the anterior and posterior branch bronchi The lumina of these bronchi were constricted but patent throughout The remaining bronchi and parenchyma were normal, and no point of perforation was visualized The pathological report was bronchogenic carcinoma, oat cell type

#### *Comment*

Selective pneumothorax, as defined by Coryllos,<sup>3</sup> means the tendency of air introduced into the pleural cavity to locate itself around the diseased parts of the lung The explanation of this process by Huist and Miller<sup>5</sup> in tuberculosis, where it is the aim of pneumothorax therapy, assumes the

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involvement of the bronchus by tuberculosis or its effects, such as edema, extrinsic pressure, etc. Then, the induction of the pneumothorax reduces the normal lengthening and shortening, and dilatation and contraction of the bronchi, and tends to completely occlude the bronchial lumen and atelectasis follows.

Selective pneumothorax, or its resultant selective collapse, is usually not considered in bronchogenic carcinoma. The position of the tumor abutting on the upper lobe bronchi, as seen in the surgical specimen, reducing the lumina but not occluding them is then analogous to the conditions in tuberculous selective pneumothorax and the explanation of the mechanism in the case presented is probably the same.

When pneumothorax with its accompanying emphysema occurs as a complication of bronchoscopy, symptoms are usually severe, and require treatment. In this case the patient was asymptomatic, and the pneumothorax was discovered on roentgen examination after the bronchoscopy. Hence, if one considered selective pneumothorax as a sign of pathology in the lung, it might be thought of as a fortunate bronchoscopic complication in this case leading to earlier thoracotomy.



FIGURE 1. Chest roentgenogram visualizes selective pneumothorax with complete collapse of the right upper lobe.



FIGURE 2 Chest roentgenogram demonstrates an infiltration in the right hilum and right upper lobe

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# Plasma Cell Granuloma of Lung\*

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A survey of the recent literature on the subject of extramedullary plasma cell granuloma of lung reveals this article to be the third published report dealing with this type of pseudotumor Childress and Adie<sup>1</sup> in 1949 and Cotton and Penido<sup>2</sup> in 1952 have preceded our own presentation with examples of a similar lesion encountered in their own patients The lesion which we report is then not only of rare occurrence but appears to be the largest of its type so far described in publication

## *Case History*

K W, a 28 year old white male, ship electrician, had suffered from persistent, moderately severe cough, productive of one ounce of semi-mucoid sputa from April to June 1951, and related one episode of minimal hemoptysis in June 1951 He had incurred no significant weight loss While in the Canal Zone in June 1951, he was informed, following a pre-employment examination, that his chest film showed a tumor in the left pericardial region and a tuberculosis-like infiltrate in the left apex He promptly returned to his home in Portland, Maine, and was studied while hospitalized there at the United States Public Health Service Hospital from July 10, 1951 to August 30, 1951 Gastric cultures for acid fast bacilli were negative He remained on outpatient status for four months and was then admitted to the Tumor Clinic, United States Public Health Service Hospital, Baltimore, Maryland for excision of the tumor in the left lower thoracic cavity Because preoperative sputas showed tubercle bacilli on smear and because it was felt prudent to obtain stabilization of the tuberculous process before attempting left thoracotomy, he was transferred to the USPHS Hospital, Manhattan Beach, New York, where he remained from February 15, 1952 to August 1952 The February 1952 chest x-ray film showed a normal right lung, in the left lung field were a fibro-exudative infiltrate in the first and second anterior interspaces and a large mass in the posterior inferior region of the pleural cavity Tomograms revealed a small cavity in the apical-posterior segment of the left upper lobe Streptomycin grams one every other day and PAS grams daily were begun February 20, 1952, INAH 300 mgm daily started August 4, 1952 and these drugs have been maintained without interruption to the present time (January, 1953)

*Past history* No member of his family was known to have had tuberculosis He further stated that as part of his duties as a ship electrician from July 1950 to March 1951 he would remove accumulated dust from the carbon brushes of the ship generators periodically, an act which caused some irritation of the naso-pharynx During the years 1948 to 1950 he worked as a hardware salesman, spending a great deal of his time in the San Joaquin Valley, California, but he had felt in good health during this period An earlier chest film in June 1950 was reportedly negative However, it is quite possible the tumor was so small at that time that its presence on a posterior-anterior projection was concealed by the then larger cardiac silhouette

By August, 1952 the left apical cavity had closed the left upper lung infiltrate had sufficiently cleared and stabilized He was transferred to the USPHS Hospital, Staten Island for left thoracotomy He was well-developed and presented no significant abnormality on physical examination—even of the chest Blood pressure 106/60

Laboratory work (prior to surgery) Leukocyte count 7500 Hemoglobin 15 Routine urine analysis was normal VDRL and Mazzini—negative Sputa smears—negative for acid fast bacilli Barium swallow showed no esophageal abnormality, no evidence of hiatus hernia (see figures 1 and 2) Electrocardiogram showed non specific T and ST wave changes—suggesting an abnormality localized to the posterior myocardium or pericardium Histoplasmin and coccidioidin skin tests were negative

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It was the impression of the surgeons that the upper lobe infiltration was tuberculous and that the mass in the lower lung field was a benign tumor. Left thoracotomy was performed on August 28, 1952. The upper lobe collapsed readily but the lower lobe maintained most of its configuration. Throughout the upper lobe could be palpated aggregates of nodular disease most numerous in the apical-posterior segment, presumably tuberculous. Occupying the central portion of the lower lobe was a firm, multilobular mass which displaced and compressed adjacent lung parenchyma in some areas and in others presented a glistening, yellow appearance beneath the visceral pleura. The inferior pulmonary ligament was abnormally and highly vascularized. Several small mediastinal nodes were present. Left lower lobectomy was performed and to prevent overexpansion of the residual lobe a tailoring thoracoplasty—periosteal, stripping of ribs one and four, resection of posterior-lateral portions of ribs two and three—was completed. The postoperative course was uneventful and he made a rapid convalescence.

*Gross description of the excised specimen.* Specimen consists of a lower lobe of lung which weighs 380 grams and measures 14.5 x 6.5 x 9.0 cms. Pleural surfaces are smooth and glistening. There is a well circumscribed but unencapsulated 9.0 x 5.0 x 4.0 cms dumb-bell shaped firm tumor mass occupying the lower two-thirds of the lung. The surrounding lung tissue is compressed but otherwise appears normal. The tumor shows no intimate relationship to adjacent lung parenchyma or regional segmental bronchi. When removed from lung it weighs 198 grams. It is fibrocartilagenous in consistency and cuts with a firm, gritty resistance. The cut surface bulges slightly and appears somewhat whoiled, and is white to cream-tan in color. No major vessels are seen leading to tumor or are lying on its cut surfaces. Minute spicules of ossified material occur in its central portion. Several submitted lymph nodes (hilary) measure up to 0.4 x 0.4 x 0.6 cm and are fleshy on cut surface. Note figure 3.

*Microscopic description.* Sections show neoplasm which is well separated from adjacent normal lung parenchyma but lacks a definite capsule. Within tumor there are nests and cords of cells resembling predominantly plasma cells admixed with lymphocytes. Such areas are surrounded by dense, fibrous connective tissue bands. No major blood vessels are seen histologically. Some sections reveal small areas of calcifications within dense fibrous connective tissue. The sectioned lymph nodes reveal mild chronic reactive hyperplasia. Figures 4 and 5.

Additional studies were made postoperatively because of the unusual gross and microscopic characteristics of the tumor suggested kinship to other diseases of tumoral, metabolic, or inflammatory etiology. Skeletal survey of skull, spine, and long bones showed no abnormality. Urine showed no Bence-Jones protein. Cholesterol determinations were within normal limits. Acid phosphatase 0.2 B U. Alkaline phosphatase 2.8 B U. Total protein 8.2 grams per cent. N P N—48 mgm per cent. Aspiration from the right iliac crest revealed normal bone marrow.



FIGURE 1



FIGURE 2

Figure 1 In this pre-operative chest film note the density lateral to the left cardiac border—Figure 2 The esophagus is visualized by barium. The arrows indicate the extent and location of this lesion.

He is still in the hospital (January, 1953) receiving appropriate therapy and making satisfactory progress in overcoming pulmonary tuberculosis. The operative procedure had no detectable adverse effect upon the status of this disease.

### *Discussion*

In a comprehensive review of the literature, Hellwig<sup>3</sup> in 1943 reported 127 cases of extramedullary plasmacytoma to which he added one of his own. In a personal communication Dr F W Stewart mentioned to him that he had observed two others. Of these, 110 occurred in the air passages and conjunctiva, however, they may occur in the digestive tract or soft regions of the body. Although they are usually single, they may be multiple. Often they are benign and do not lead to metastases except in rare cases to regional lymph nodes. Histologically, plasmacytomas have



FIGURE 3 Gross appearance of tumor occupying  $\frac{2}{3}$  of left lower lobe

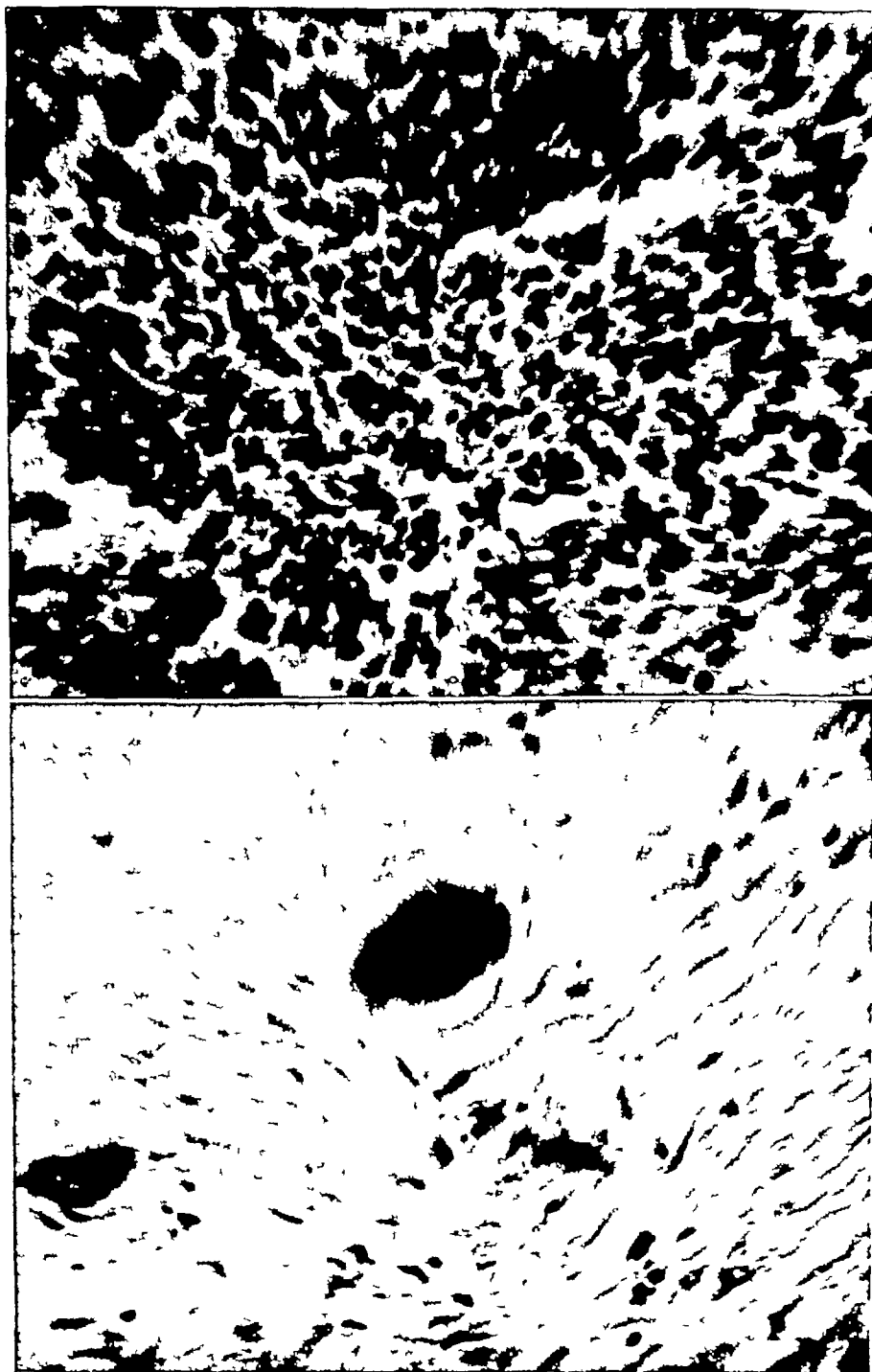


FIGURE 4, *above* Areas of tumor with nests of round cells in which plasmal cell predominates H & E stain high dry power field

FIGURE 5, *below* Areas of calcification in dense fibrous connective tissue within tumor H & E stain 400X

the appearance of true primary tumors consisting solely of plasma cells. This type can be classified as a plasma cell tumor. Another type which has been described consists mainly of plasma cells, but lymphocytes, leucocytes, and fibroblasts are also present. This form should be differentiated from the tumoral type and preferably should be considered a plasma cell granuloma.<sup>4</sup> The latter occurs in areas of focal infection. The presence of plasma cells in chronic inflammatory conditions is well known.

Xanthomatous tumors are distinct both morphologically and histologically from plasmacytomas being characterized by the presence of foam cells in addition to chronic inflammatory cells. Grossly they are golden-yellow. The isolated xanthomata of lung reported by Scott<sup>5</sup> in 1948 and Ford<sup>6</sup> in 1950 showed no abnormality in the serum cholesterol. Although the diagnosis of xanthoma was not entertained in our case, we point out that our patient's cholesterol and cholesterol esters were within normal limits. No foam cells were seen in our lesion.

Plasma cells in plasmacytoma resemble myeloma cells. They have characteristic eccentric nuclei which reveal clumped chromatin in a cartwheel like appearance.

The cytoplasm is mildly to strongly basophilic. The origin of the plasma cell is in dispute but the concept gaining widest acceptance is that these cells arise from the myeloid tissue in the myelomas or from lymphatic tissue in the case of the extramedullary plasmacytoma and inflammatory disease, the stem cells in either case are the reticulo-endothelial cells. Multiple myelomas invariably and extramedullary plasmacytomas commonly are attended by an upset in the serum protein balance of the blood due to an increase in serum globulin. Our patient showed normal serum protein levels and a normal A/G ratio. At no time did he have albuminuria or Bence-Jones protein in the urine. Postoperative skeletal roentgen studies failed to reveal any pathology which would suggest myeloma.

Special stains failed to reveal specific organisms—namely fungi, bacteria, or acid fast bacilli. The supposition that this lesion is a coccidioidal granuloma can be eliminated because of the negative coccidioidin skin test and the absence of endospores in tissue sections. The negative venereal disease history and negative serology exclude the possibility of a luetic gumma. The coincidental occurrence of active pulmonary tuberculosis in the left upper lobe suggests tuberculosis as the specific etiologic factor. However, smears and cultures from the excised lesion were negative, and the histologic picture was not characteristic for tuberculosis.

We regard the lesion described herein as a plasma cell granuloma of nonspecific inflammatory origin because of its variable composition with a preponderance of plasma cells.

#### SUMMARY

We regard the lesion described herein as a plasma cell granuloma of lung treated by lobectomy. The pseudotumor itself weighed 198 grams, measured 9 x 5 x 4 cms, and is the largest of its type thus far reported in the literature.

## RESUMEN

Presentamos un caso de "plasma cell" granuloma extramedular del pulmón tratado por lobectomía. El pseudo tumor pesaba 198 gramos, medía 9 x 5 x 4 cms, y es el mayor de su tipo hasta hoy relatado en la literatura.

## RESUME

Les auteurs rapportent une observation de granulome à cellules extra-médullaires du poumon, traité par lobectomie. Cette pseudo-tumeur pesait 198 grammes, mesurait 9 x 5 x 4 cm et est la plus volumineuse de ce type qui, jusqu'à présent, ait été rapportée dans la littérature.

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# Treatment of Air Embolism in Pneumoperitoneum

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Since the introduction of pneumoperitoneum as an adjunct in the treatment of pulmonary tuberculosis by Banyai in the early 1930's, this procedure has assumed great popularity in the various chest clinics throughout the country. Pneumoperitoneum has proved to be beneficial in bilateral pulmonary tuberculous lesions whether in the apical or basal segments of the lungs. It has been satisfactorily used as an adjunct in improving the patient's condition so that surgery, not feasible at the moment, may be performed subsequently. It has also been applicable to patients who are not eligible for other types of mechanical therapy either because of age, general debilitation or because of low vital pulmonary capacity.

At Kings County Hospital, a large general city hospital of 3000 beds, of which 700 are used exclusively for pulmonary tuberculosis, pneumoperitoneum is one of the frequently used forms of therapy both on the wards and in the clinics. The out-patient department of the tuberculosis clinic treats approximately 30 patients daily by pneumoperitoneal refills. This has been used for years without fatality. However, with such procedure as pneumoperitoneum, the thought of air embolism is ever present. With this in mind the following case is presented.

A. L., a Negro female, age 35, was discovered to have pulmonary tuberculosis in November 1947. She was admitted to Kings County Hospital for her attacks of bronchial asthma, weight loss (20 lbs.), anorexia and night sweats. Her past history was essentially negative. Her mother and father both died from pulmonary tuberculosis and her daughter had this disease. Her husband was alive and well.

X-ray film inspection in November 1947 revealed, "Caseous pneumonic tuberculous infiltration of the right upper lobe with a cavity size of 1 cm. in diameter. There is an exudative spread noted in left mid lung field." Sputum was positive for acid fast bacilli and she was placed on bed rest and dihydrostreptomycin. In June 1948 her left lung field cleared and in August 1948 pneumothorax was instituted on the right side which was discontinued in February 1949 because of right pleural effusion. In March 1949 pneumoperitoneum was instituted with good results. She was discharged to the out-patient department on September 26, 1950 for weekly refills of air (500 cc.) which were given in the right upper quadrant of the abdomen to maintain an adequate rise of the diaphragm.

On December 20, 1951 after she was fluoroscoped and found to have adequate space, a blunt 19 gauge needle was inserted into the abdominal cavity in the right upper quadrant. The syringe was manipulated and no blood was obtained. The manometric reading was plus four.

At the close of the treatment in which 500 cc. of air had been instilled, she became breathless, her eyes rolled to one side, the pulse became imperceptible and she became comatose. She was immediately placed in the left lateral position after the procedure described by Durant.<sup>1</sup> Within several minutes the pulse became stronger, the blood pressure started to rise, although she still remained unconscious for three quarters of an hour and had incontinence of urine and feces. Within this 45 minute period she revived and was admitted to the hospital. There was no evidence of neurological signs. Her reflexes were normal.

She was discharged from the hospital on December 22, 1951 at which time she complained of numbness from her diaphragm to her extremities. Since then her numbness has disappeared. In her own words before she became unconscious she said, "I felt air going around in a circle and then I passed out."

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*Comment*

In pneumoperitoneum an embolism occurs as a result of the entrance of massive quantities of air into a systemic vein which is transported to the right heart and thus produces an acute mechanical obstruction to the outflow tract of the right ventricle. Durant has proved by experimental procedures on dogs that the obstruction of the outflow tract of the right ventricle due to air embolism can be relieved by placing the individual in the left lateral position, so as to allow the air mixed with the blood to churn into froth. Thus the blood is transported into the lungs where excretion occurs. The procedure as described by Durant was the one used in the above case. Our patient did not receive any other form of therapy such as oxygen or stimulants.



FIGURE 1

## SUMMARY

1 A case of an embolism has been presented with treatment after that described by Durant

2 This procedure described by Durant and his associates in placing the patient in left lateral position after venous air embolism should be constantly in the minds of those clinicians who give pneumoperitoneum treatments, in order to avoid fatalities

## RESUMEN

1 —Se presenta un caso de embolia gaseosa en el que se empleó el tratamiento descrito por Durant

2 —Este procedimiento descrito por Durant y sus asociados consistente en colocar al enfermo en decúbito lateral izquierdo cuando ocurre la embolia, debe tenerse siempre presente por los clínicos que hacen neumoperitoneo a fin de evitar los casos fatales de embolia

## RESUME

L'auteur présente un cas d'embolie gazeuse dont le traitement a été institué selon la technique de Durant

Cette méthode qui consiste à placer le malade en position latérale gauche après embolie gazeuse d'origine veineuse, devrait être constamment présente à l'esprit des cliniciens qui pratiquent des pneumopéritoneums afin qu'ils puissent éviter les accidents mortels

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# Cavitation in Metastatic Pulmonary Neoplasm

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Necrosis and cavitation are a frequent occurrence in primary tumors of the lung<sup>1, 4</sup> However, pulmonary cavitation of a metastatic nodule in the lung is rare Dolgoff and Hansen<sup>5</sup> in a survey of the literature did not find a previously recorded example of such an occurrence Others<sup>6, 7</sup> however, have reported cavernous lesions in metastatic carcinomas More recently<sup>8</sup> two additional cases were reported, showing multiple cavitation The following case is described in order to call attention to metastatic disease in the differential diagnosis of pulmonary cavities

A Z, a dentist, age 66, was admitted to the Jewish Memorial Hospital on April 5, 1951, with the history of acute upper respiratory infection for seven weeks prior to admission This was accompanied by slight cough with scanty expectoration, and sore throat He ran a low-grade fever up to 102° for several days prior to admission His presenting complaint was that of extreme weakness and dizziness He further complained of increased constipation and black stool, and weight loss of 12 lbs He had been operated upon at the Mt Sinai Hospital, New York City, eight years before for obstructing adenocarcinoma of the transverse colon

Physical examination revealed a middle-aged white male who appeared chronically ill There was dullness over the upper lobe of the right lung, with occasional scattered rales over both bases Examination of the heart was negative Liver, kidney and spleen were not palpable There were no palpable glands Blood count on admission showed hgb 6.5 gm, red blood cells 1,900,000, with achromia, anisocytosis and microcytosis A sternal marrow puncture was done two days after admission This revealed a myeloblastic picture

Roentgenological examination revealed multiple nodular lung densities with atelectasis The hilar glands were enlarged and the right upper lobe showed a pneumonic density suggestive of atelectasis, at the outer aspect of which a cavity could be seen (Fig 1)

He developed epistaxis and transfusions were given His condition became worse, and despite supportive measures, he died three weeks after admission Three days before death, he developed an enlarged spleen and petechiae The white count rose to 129,000 and the platelets fell to 70,000

The following pertinent necropsy findings were noted in the lungs

The left lung was aerated and on cut section showed several discrete rounded nodular tumor masses with marked central necrosis The right lung was bulky The right upper lobe was taken up by a large solitary nodular rounded tumor mass with marked central cheesy necrosis measuring 4 cm in diameter The right middle lobe showed a similar solitary nodular tumor 1½ cm in diameter

Microscopic examination showed invasion and replacement by markedly atypical glandular epithelium with marked disorientation of the nuclei Extensive secondary degeneration and necrosis was present Other section showed extensive intraalveolar mononucleosis and heart failure cells with septal and alveolar elements Some sections showed extensive pneumonic infiltration with surrounding hemorrhage and necrosis of lung parenchyma Other sections showed extensive interstitial leukemic infiltrations consisting of very young large myeloid cells

Summary of autopsy findings Metastases to the lungs from a primary adenocarcinoma of the transverse colon in a patient who developed a superimposed acute leukemia

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The authors thank Dr Milton A Miller for permission to publish this case  
Attending Physician (Dr Bass)  
Adjunct Physician (Dr Katzev)



## SUMMARY

1 A case of cavitation in a metastatic pulmonary neoplasm has been described

2 Metastatic disease should be considered in the differential diagnosis of pulmonary cavitation

## RESUMEN

1 Se describe un caso de neoplasia metastática pulmonar excavada

2 La metástasis neoplásica, debe tomarse en cuenta en el—diagnóstico diferencial de la excavación pulmonar

## RESUME

Les auteurs décrivent un cas de métastase néoplasique pulmonaire dans laquelle s'est creusée une cavité

Il faut envisager le cancer secondaire quand on discute le diagnostic des cavernes pulmonaires

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# Editorial

## ISONIAZIDS VERSUS STREPTOMYCIN

A critical appraisal of the use of isoniazids versus streptomycin has been difficult to evaluate. Everybody is willing to admit that both the chemical drug and the antibiotic are wonderful adjuvants in the treatment of tuberculosis. An attempt has been made to compare the results of the treatment with isoniazids or streptomycin in a mass survey of patients treated in various institutions. Such a comparison immediately brings up the question of the variations in the duration and the character of the pulmonary disease, and the dosage used. Results would not be uniform if too low or too large a dose was used.

Direct comparison of cases is not the answer! Isoniazids had many successful results in streptomycin failures. Isoniazids alone, or with synergists, appear to have good results. There should not be an impression that streptomycin may have a kindred value to isoniazids for streptomycin is less certain of obtaining an arrest of the tuberculous disease.

However, physicians are being advised that streptomycin and para-aminosalicylic acid are the drugs of choice, and if the patient does not respond well, then isoniazids should be used. Unfortunately, because of the better results in isoniazids, this 'wait and see' policy is wrong. The 'wait and see' period is about six months, and in that time the disease might very well have been controlled with isoniazids.

Isoniazids do well alone, and better with synergists. If isoniazids are used, the synergist of choice is dihydro-streptomycin or streptomycin. Remember, the antibiotics are used, though alone they are more apt to be failures. The antibiotics are really synergists, increasing the action of isoniazids over what it may accomplish alone. The next synergists are PAS and terramycin but to a lesser extent than dihydro-streptomycin and streptomycin.

The arrest of tuberculosis is the goal in treatment. Collapse therapy (pneumothorax or pneumoperitoneum, when indications require such treatments) used simultaneously with isoniazids and synergists should begin on the same day.

Our interest is not to determine which form of therapy could be responsible for the arrest of the disease but just to accomplish such an arrest.

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# Teaching Chest Disease\*

## The Importance of the Physiology Laboratory in the Teaching of Diseases of the Chest\*\*

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Pulmonary physiology is divided into clinical and theoretical fields of study more sharply than almost any other medical specialty. It originated as a theoretical study at least 75 years ago, during the last half of the nineteenth century, in the many basic observations on the mechanics ventilation recorded by physiologists in France and England. The development of chemical methods of analysis in the first quarter of this century, by Van Slyke, Henderson, Haldane and others, was revolutionary, making possible vast strides in our knowledge of the behavior of blood and alveolar gases. During the last 25 years, our understanding of pulmonary physiology has been consolidated and expanded. The development and refinement of new techniques of investigation, upon which theoretical physiology depends, has been carried on by Cournand, Richards, Riley and a host of other scientists.

This has been inevitably a process of specialization, accompanied by the gradual growth of concepts and terminology peculiar to itself. As a result, the literature on pulmonary physiology is formidable. It is also apt to appear to be somewhat remote from clinical medicine. Papers on detailed techniques of study are of great interest to physiologists but they make the clinician feel that the subject is so complicated that he cannot understand it, and that the facilities for such study are not generally available anyway.

Meanwhile, pulmonary physiology has become a subject of great clinical importance recently, with the advances of thoracic surgery. Its significance was underlined by the discovery that an operation which was life-saving for one patient might turn another into a complete respiratory cripple. At the present time, almost every patient considered for thoracic surgery should undergo a series of tests of pulmonary function. The results of such studies will affect the kind of surgery to be undertaken, the limitations upon excision which must be observed, or even be in themselves an absolute contraindication to any surgical procedures on occasion.

In response to this need for regular clinical evaluation of pulmonary function, simple methods of clinical assessment have been developed by Waring, Gaensler and others. These tests were devised for ease of administration and interpretation and simplicity of equipment. The theoretical work of Cournand, Richards and many others was of great value.

\*The second in a new series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians.

\*\*From the Department of Medicine, University of California School of Medicine and the San Francisco Department of Health, San Francisco Hospital.



in the development of these simplified procedures, particularly in providing scientifically-determined limits of normality against which the amount of dyspnea in any individual case could be accurately estimated

In the last five years, the clinical application of pulmonary function tests has been greatly extended. They can be of nearly daily service to any physician in his treatment of chronic lung abnormalities, such as emphysema and pulmonary fibrosis, since they are almost the only way of objectively estimating the efficacy of drugs and other therapeutic procedures upon dyspnea. Beyond this, such tests can be of great use in diagnosis, since they provide information as to the type of functional disability resulting from a given pulmonary lesion.

This further clinical application has been made the question of simplicity and inexpensiveness of equipment even more important. It is now apparent that a useful laboratory requires small expenditure. Some kind of low-resistance spirometer, gas meter, Douglas bag and appropriate valves and connections can provide all the basic information that is usually required, although further equipment may be useful even in daily office routine.

In medical school one cannot of course, ignore either of the directions of pulmonary physiology, the theoretical or the clinical. But we believe that the emphasis must be upon the latter. A competent clinician should know enough about the more complex functional tests to make use of the information that they can provide, although he will rarely be called upon to administer such tests himself. On the other hand, the information to be obtained from the use of simple procedures will be adequate in the great majority of cases. After all, one does not think of cardiac catheterization, ballistocardiography and angiocardigram in physiologic evaluation of the average case of cardiovascular disease. One uses simple physiologic studies of blood pressure, heart rate, vital capacity, exercise tolerance, body weight and other readily measurable phenomena. Pulmonary physiology should be taught in the same way. In the average dyspneic patient we do not measure gradients for oxygen, venous admixtures and so forth but can obtain basic information by simple ventilatory studies. The student should be trained to think of pulmonary physiology as an integral aspect of his practice of clinical medicine.

Students at the University of California School of Medicine are expected to master the basic principles of pulmonary physiology during their general physiologic training period, and in special courses in cardiology. From the beginning, clinical application is stressed and clinicians take part in the presentation of the normal academic course.

Students are then introduced to the clinical physiology laboratory during their later years of training. This laboratory is operated in connection with the University Tuberculosis Division, which maintains about 200 beds. While on the service the students see demonstrations of pulmonary function studies and are encouraged to act as "guinea-pigs" to see how the tests work. They also attend ward conferences on medical and surgical patients on whom studies have been done. Physiologic considerations

are stressed in these conferences. There are formal discussions of problems of dyspnea from the basic physiologic as well as clinical point of view, together with practical demonstrations of newer aids in treatment, such as intermittent positive pressure breathing. They follow lesions in their clinical progress and correlate this progress with physiological consequences by means of repeated pulmonary function tests. Therapy is evaluated in the same way. Thus, it is hoped, students will learn to integrate bacteriological, pathological and clinical findings into a broad understanding of symptoms, including dyspnea, in relation to the impaired function which is their origin.

We believe that teaching chest disease has many facets, none of which can be neglected if training in total patient care is to be our aim. The great effort of medical schools today is to translate the theoretical into the practical. Bacteriology is taught in the laboratory and clinical epidemiologic problems in the wards. Pathology is taught at the microscope and translated at the bedside into an understanding of the tissue changes underlying clinical states. Anatomy is taught in the dissecting room and applied in clinical interpretation of x-ray films. As with these older established fields, so physiological tests are conceived in the laboratory and developed into aids for the greater clinical understanding of the disease processes underlying such symptoms as cough and dyspnea. Thus physiological tests contribute to the broad outlook on disease which is one of the distinguishing characteristics of modern medicine.

# The President's Page

## THE COMMON BOND

The first cry of pain at the dawn of time brought from the victim's fellowman an expression of concern for the relief of the individual in distress. This concern for the welfare of a fellowman is a dominant characteristic of the human race.

The care and attention given to the ill or injured in early times were crude and were, at times, ineffectual, but, each succeeding experience afforded an increasing fund of knowledge concerning the ailments to which man was subject. Some men were more adept in their administrations and through service developed a better understanding of the various ailments with which man was afflicted, they came to be known as physicians.

Physicians found it helpful to discuss their problems with similarly minded men of their community. In time, information was exchanged with men outside the immediate neighborhood, and, finally, the physician found himself traveling into distant lands in search of knowledge and skills, to be used in the care of the sick and injured at home. This search for information often took the physician into enemy countries. The appeal of the sick and injured was the foundation for the development of a universal understanding and common purpose for all physicians. Friend and foe could meet on this common ground without the introduction of discordant matters. A liberal exchange of medical knowledge and skills between physicians has always prevailed. It has been the usual custom for physicians to treat friend and enemy alike, there being no limit to the bounty of their services.

The American College of Chest Physicians was founded by a group of physicians who were motivated by the same compelling urge as their forefathers to search for means to better serve mankind. They sought to make available for the physicians of their communities, knowledge and information regarding diseases of the chest and thereby to increase their capacity for service. Throughout the years this ideal has continued to be the fixed purpose of those who make up the college.

To further promote the free exchange of knowledge and skills, concerning diseases of the chest between physicians on a world-wide level, an "International Congress on Diseases of the Chest" was organized. No political nor geographical boundaries were to limit the exchange of knowledge.

The first International Congress on Diseases of the Chest was held in Rome, Italy in 1950. At this congress we participated in a liberal exchange of knowledge and skills between physicians from all over the world. Each returned to his homeland with the conviction that he could better serve his fellowman at home as a result of the liberal and unselfish exchange of information that had taken place at Rome. Each returned home a little less ready to condemn what might have been considered short-comings of his fellow physicians and, with a better understanding of the medical problems of his conferees in other lands. The universality of the language (cry) of the distressed, as it is interpreted by the physician, has been reaffirmed at the Second International Congress in Rio de Janeiro and, more recently, at the Third International Congress in Barcelona, Spain. Many physicians traveled thousands of miles to attend these International Congresses. No patents nor copyrights interfered with the liberal exchange of medical information. Each physician gave freely of his knowledge and skills. Meeting as we did on a common ground of mutual accord to discuss matters universal in their appeal has resulted in a better understanding between individuals of many lands.

The friendships which have developed through these meetings are solid and enduring. Political and geographical boundaries may restrict physical contact between physicians but their unselfish service to humanity is creating an enduring monument to physicians and to the invisible but strong bonds which unite them in their common purpose of improving and expanding service in the relief of afflicted humanity.

*William A. Hudson*

## Outstanding Scientific Program for 21st Annual Meeting

Dr Burgess L Gordon, Philadelphia, Chairman of the Committee on Scientific Program for the 21st Annual Meeting of the American College of Chest Physicians, has announced that the program is in its final stages of completion and will be available for publication in the March issue of DISEASES OF THE CHEST. Be sure to look for the final program in the March issue. The annual meeting will be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2 through 5, 1955.

Many innovations, which are certain to be of unusual interest to our members, have been made in the program this year. There will be a number of panel discussions and considerably more than the usual amount of time for discussion from the floor has been planned. Prominent speakers will present concise reports of their studies in special fields such as cancer, emphysema, pulmonary and cardiac function, heart and thoracic surgery, tuberculosis and nontuberculous diseases of the chest, industrial diseases, and many others, and the question-and-answer periods will be open to all interested physicians.

On Friday evening, June 3, the "Fireside Conferences" will be held with more than thirty subjects to be discussed, covering a wide range of almost every conceivable aspect of chest disease—more than enough to interest everyone—with refreshments to assist in keeping the discussions going. An outstanding scientist will lead the discussion of each subject and hosts will be on hand to direct and introduce, and generally aid in engendering the feeling of good fellowship.

The first "Selman Waksman Lecture," sponsored by the New Jersey Chapter of the College, will be presented on the opening night of the meeting, Thursday, June 2, and the guest speaker will be Sir Geoffrey Todd, Medical Director of the King Edward VII Sanatorium, Sussex, England, an outstanding authority. His subject will be "Modern Concepts of Tuberculosis."

A Diagnostic-Treatment Conference will be presented on Saturday afternoon, June 4. Members will have the opportunity of selection from a group of six popular round table luncheon discussions to be presented on each of three days of the meeting, Friday, Saturday and Sunday, June 3, 4 and 5. Motion picture sessions on diseases of the chest will be presented concurrently with the scientific sessions on these days.

Examinations for Fellowship in the College will be held on Thursday, June 2. The annual Seminars, which have been accredited by the Board of Examiners for candidates for Fellowship in the College, will be presented on Wednesday, June 1.

Meetings of all councils and committees of the College will be scheduled for Thursday, June 2, at the Ambassador Hotel. Members of the College councils and committees are urgently requested to make plans to attend these important meetings.

Honorary Fellowship in the College will be conferred upon a number of prominent scientists at the annual Convocation to be held on Saturday evening, June 4. This will be followed by a cocktail party and the Annual Presidents' Banquet. There will be no speeches. Dancing and good fellowship will conclude the evening.

Mrs Irving Willner, Newark, New Jersey, Chairman of the Ladies Reception Committee, has announced that there will be an enjoyable program of events for the ladies attending the meeting.

A hotel reservation form may be found on page xvi of this issue of the journal and it is suggested that this form be mailed at once to the Ambassador Hotel. Reservations will be accepted in the order in which they are received and to be assured of accommodations for the meeting at the headquarters hotel, it is advisable that you fill out the coupon and mail it today. The American Medical Association will meet in Atlantic City, June 6-10, 1955. The Section on Diseases of the Chest will meet on June 7-8-9. When completing your hotel reservation form, please give arrival and departure dates.

## College Interim Session

More than 250 physicians and guests were present in Miami Beach, Florida, on Sunday, November 28 for an excellent scientific program sponsored by the Florida Chapter of the College. The chapter also sponsored a cocktail party on Sunday evening, followed by a dinner presided over by Dr Alexander Libow, Chairman of the Scientific Program Committee. Dr Libow introduced Dr William A Hudson, President of the College who spoke on the Third International Congress on Diseases of the Chest held recently in Barcelona, Spain. Dr M Jay Flipse, Regent of the College for Florida, served as moderator for the diagnostic-treatment conference which followed the dinner. The members of the committees were complimented by the Board of Regents for the arrangement of a splendid meeting.

The Executive Council, Board of Regents and Board of Governors of the College held meetings at the Delano Hotel, Miami Beach, on Monday, November 29. The following College officials and guests attended these meetings:

William A Hudson, Detroit, Michigan, President  
Donald R McKay, Buffalo, New York, Chairman, Board of Regents  
David H Waterman, Knoxville, Tennessee, Chairman, Board of Governors  
Arnold S Anderson, St Petersburg, Florida  
Albert H Andrews, Chicago, Illinois  
Charles P Bailey, Philadelphia, Pennsylvania  
Otto L Bettag, Chicago, Illinois  
Charles A Blasher, Mount Vernon, Missouri  
Benjamin L Brock, Orlando, Florida  
Maurice Campagna, New Orleans, Louisiana  
Duane Carl, Memphis, Tennessee  
Alberto Chattas, Cordoba, Argentina  
Ross K Childerhose, Harrisburg, Pennsylvania  
Dean B Cole, Richmond, Virginia  
DeWitt C Daughtry, Miami, Florida  
M Jay Flipse, Miami, Florida  
Carl H Gellenthien, Valmora, New Mexico  
Burgess L Gordon, Philadelphia, Pennsylvania  
Edward A Greco, Portland, Maine  
Alvis E Greer, Houston, Texas  
J E J Harris, Albuquerque, New Mexico  
Willard B Howes, Detroit, Michigan  
Chevalier L Jackson, Philadelphia, Pennsylvania  
Hollis E Johnson, Nashville, Tennessee  
Edward Lebovitz, Pittsburgh, Pennsylvania  
Edwin R Levine, Chicago, Illinois  
Alexander Libow, Miami Beach, Florida  
Francisco J Menendez, Havana, Cuba  
Arnold Minnig, Denver, Colorado  
Herman J Moeisch, Rochester, Minnesota  
Jay Arthur Myers, Minneapolis, Minnesota  
J Winthrop Peabody, Washington, D C  
Charles K Petter, Waukegan, Illinois  
David B Radner, Chicago, Illinois  
Jack Reiss, Coral Gables, Florida  
Alfred A Richman, New York, N Y  
William R Rumel, Salt Lake City, Utah  
James H Stygall, Indianapolis, Indiana  
Harold G Trimble, Oakland, California  
Buford H Wardrip, San Jose, California  
Murray Kornfeld, Chicago, Illinois, Executive Director  
Harriet L Kruse, Chicago, Illinois, Executive Assistant

## JOINT MEETING BOARD OF REGENTS AND BOARD OF GOVERNORS

A joint meeting of the Board of Regents and Board of Governors was held at the Delano Hotel, Miami Beach, at 10 30 a m on Monday, November 29 Dr David H Waterman, Chairman of the Board of Governors, presided The following reports were presented

### Council on Postgraduate Medical Education

Since the annual meeting of the College held in San Francisco last June, three postgraduate courses on diseases of the chest have been presented under the sponsorship of the Council on Postgraduate Medical Education of the College

During the week October 18 through 22, the Ninth Annual Postgraduate Course was presented at the Knickerbocker Hotel, Chicago, which was attended by forty physicians A three day postgraduate course was presented in Cleveland, Ohio, October 27-29, under the auspices of the Cleveland Clinic This course was attended by sixty physicians The third course was the Seventh Annual Postgraduate course presented at the Hotel New Yorker, New York City, November 8-12, at which one hundred and two physicians were registered All of these courses were well presented and the comments received from the physicians who participated were most favorable

The postgraduate course committee in Philadelphia has announced the completion of the program for the Eighth Annual Postgraduate Course to be held there, in cooperation with the Laennec Society of Philadelphia, March 7-11, 1955 An excellent curriculum has been prepared for this course and copies may be obtained by writing to the Executive Offices of the College in Chicago

J WINTHROP PEABODY, *Chairman*

### Council on Undergraduate Medical Education

During the past year, the Council on Undergraduate Medical Education of the College has sponsored the publication of a number of articles on the teaching of diseases of the chest in the official journal of the College, DISEASES OF THE CHEST We are pleased to announce that this series of articles will be continued in the coming year Dr Theodore H Noehren, Vice Chairman of the Council, who contributed several articles to the series, has sent letters to many physicians engaged in teaching chest diseases, describing the program The Council will be pleased to hear from members of the College who may have something to contribute to this phase of our program The Council has requested the Committee on Motion Pictures to review and recommend motion pictures suitable for teaching undergraduate medical students

With regard to the Committee on College Essay, which serves under our Council, a release concerning the 1955 Prize Essay Contest of the College has been printed and widely distributed Members of the College who are affiliated with teaching institutions are requested to bring this Contest to the attention of medical students

In the past, one prize of \$250 00 and a certificate of merit was awarded the winner of the Contest, with the second and third prize winners receiving appropriate certificates At the last annual meeting of the Council it was recommended, and subsequently approved by the Board of Regents, that for the 1955 Contest there be three monetary prizes, the first prize to be \$250 00 and a certificate of merit, second prize \$100 00 and a certificate of merit, and a third prize of \$50 00 and a certificate of merit Applications for entry in the Contest may be obtained by any student in an approved medical school by writing to the Executive Offices of the College in Chicago

EDWARD W HAYES, *Chairman*

## Committee on Resident Fellowships

In June, 1951, with the approval of the Board of Regents of the College, the Committee on Resident Fellowships in Chest Diseases was established for the purpose of assisting qualified physicians throughout the world in receiving postgraduate training in the recent advances in the diagnosis and treatment of heart and lung diseases.

Immediately after the establishment of administrative procedures, the Committee, with the aid of the Executive Offices of the College, undertook the task of corresponding with appropriate medical institutions in the United States which maintain chest clinics or hospitals and sanatoria established for the purpose of treating tuberculosis and allied disorders. The response was gratifying as many institutions offered interesting residencies, including full maintenance in addition to a small stipend. As soon as these institutions indicated their willingness to accept Resident Fellows, officials of the College throughout the world were notified of the available opportunities which existed for postgraduate training. The officials were supplied with appropriate application forms, and within a very short period thereafter, the Committee on Resident Fellowships had the difficult task of screening the many applications that were received.

To facilitate the many problems encountered in obtaining visas, the American College of Chest Physicians applied for an Exchange Visitors Program number which, we are pleased to report, was approved by the Department of State.

During the past 3 years, the Committee on Resident Fellowships has received 130 requests for information. Ninety-eight applications were filed, of which 70 were approved by the Committee after having been previously approved by the Governors and Regents of the College in the respective countries. As of this date, 38 physicians have received or are at present receiving postgraduate training in diseases of the chest in this country. These physicians have come from the following countries: South Africa, England, Japan, India, Brazil, Spain, Panama, Nicaragua, Chile, Israel, Argentina, Formosa, Austria, Turkey, Peru, Korea, Costa Rica, the Philippines, Greece, Portugal, Italy, and Egypt.

This program has been highly commended by the Pan-American Sanitary Bureau, the United States Department of State, the American-Korean Foundation, and other government and private organizations.

A resolution was adopted by the Board of Regents at their meeting in St. Louis, Missouri on November 30, 1953, to prepare a certificate for Resident Fellows who have completed their training under the sponsorship of the Committee on Resident Fellowships. These certificates are now being awarded in accordance with this resolution.

It gives me a great deal of pleasure to announce that a special room at the Manhattan General Hospital is being set aside for the permanent New York City Headquarters of our committee. It is planned to have desks, chairs, telephone, writing materials and other conveniences at hand for the use of visiting Resident Fellows. A special plaque is also being prepared stating the purpose and sponsorship of the room, which will be installed on the door. Physicians are invited to make use of this room during their visits to New York City.

ALFRED A. RICHMAN, *Chairman*

The Regents and Governors extended their appreciation to Dr. Richman for the donation of the Headquarters Room at the Manhattan General Hospital and expressed the hope that headquarters will soon be established in other cities for this purpose.

### Committee on Membership

At the time of the annual meeting in June 1954, the total membership of the College was 4787. There are now 279 applications for membership to be presented to the Board of Regents for approval at this meeting. Of this number, 140 are for Fellowship, 38 for Associate Fellowship, 79 for Associate Membership, 20 for Advancement to Fellowship and 2 for Advancement to Associate Fellowship. Of the 279 applications, there are 145 from the United States and Canada and 134 from other countries.

In addition to the above applications, there are now 62 applications filed between September 15 and November 15, 1954, which will be presented to the Board of Regents in June 1955.

CHEVALIER L. JACKSON, *Chairman*

### Committee on College Chapters

During the interim between our annual and semi-annual meetings, several of our chapters have held very successful meetings.

The Rocky Mountain Chapter, which includes the states of Colorado, New Mexico, Utah and Wyoming, met at the Broadmoor Hotel on Saturday, September 25. Forty-five physicians attended and a splendid program was presented. Dr. Albert H. Andrews of Chicago and Dr. John S. Chapman of Dallas were invited as guest speakers in addition to other speakers from the chapter.

The Wisconsin Chapter met in Milwaukee on October 3 and 178 physicians attended. The well-planned scientific program was enthusiastically received.

The North Carolina Chapter met concurrently with Hurricane Hazel in Winston-Salem on October 15. In spite of the fact that Winston-Salem lay in the direct path of the hurricane, thirty physicians attended the meeting and an excellent scientific program was presented. Dr. Francis M. Woods of Brookline, Massachusetts, was the guest speaker for the evening session. The chapter deserves our congratulations for proceeding with its meeting in the face of great difficulty.

ALVIS E. GREER, *Chairman*

Dr. Hudson presented a report of the international activities of the College, including a brief resume of the excellent meetings of the World Medical Association and the International Bronchoesophagological Society which he attended in Rome and Lisbon, respectively, during the months of September and October as an official representative of the American College of Chest Physicians. Dr. Hudson stated that during his visits in Rome and Lisbon, as well as in Barcelona for the International Congress of the College, the many physicians he met expressed great interest in the Resident Fellowship program of the College and felt that this was a most worthwhile activity. The President stated that he hoped a good number of the Regents and Governors, as well as other members of the College, were planning to attend the meeting of the Cuban Chapter to be held in Havana on December 1. He pointed out that an excellent scientific program would be presented at the chapter meeting and that the officials and members of the Cuban Chapter had planned a most interesting and enjoyable social program for the College group.

Dr. Hudson announced that the Fourth International Congress on Diseases of the Chest, sponsored by the Council on International Affairs of the College, would be held in Cologne, Germany, in 1956.

Dr. Gordon, Chairman of the Committee on Scientific Program for the 21st Annual Meeting of the College, gave a brief outline of the plans for the scientific program. He announced that a number of innovations for the Atlantic City meeting had been planned, such as "Fireside Conferences," motion picture programs, adequate time for discussion from the floor, many panel discussions and summarization.



The following correspondence was read

A letter received from Henrietta McNary, President of the American Occupational Therapy Association, concerning the first meeting of the Medical Advisory Council, to which Dr Leonard C Evander, Lockport, New York, has been appointed as the representative of the College

A copy of a letter written by Dr Edward C Holmblad, Executive Director of the Industrial Medical Association, to Dr Arthur Voiwald, stating that their Association will appoint a committee on rehabilitation to consult with the College committee when problems of mutual concern arise

A vote of thanks was extended by the Regents and Governors to all of the committees responsible for the successful meeting held in Miami Beach, to the ladies committee for the splendid program they had arranged for the visiting doctors' wives and families, to Dr Jack Reiss on the excellent program prepared for the Chest Section of the American Medical Association meeting, and to the staff of the Delano Hotel for their courtesy and cooperation during the meeting Adjournment

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### SEMI-ANNUAL MEETING BOARD OF REGENTS

The semi-annual meeting of the Board of Regents was held at 2 00 p m on Monday, November 29, at the Delano Hotel, Miami Beach Dr Donald R McKay, Chairman of the Board, presided

Dr Pettei, the Treasurer of the College, presented the financial report, proposed 1955 budget and the report of the Committee on Insurance, of which he serves as Chairman Upon motion duly seconded, the above reports were approved

The report of the Committee on Physiologic Therapy was presented by the chairman, Dr Andrews The committee requested that the Board of Regents of the College sponsor the newly organized American Association of Inhalational Therapists Dr Andrews submitted the by-laws of this society to the Board of Regents which had been prepared under the guidance of the committee The Board was of the opinion that this association could serve a useful purpose and agreed to sponsor the society in accord with the recommendations and stipulations set forth by the Committee on Physiologic Therapy The committee also requested permission to present its exhibit at the annual meetings of the College and the American Medical Association in Atlantic City in June, 1955 This request was approved

Dr John F Briggs, St Paul, Minnesota, was unable to be present at the meeting, Dr Briggs' report of the Committee on Cardiovascular Disease, of which he serves as chairman, was read

"The Committee on Cardiovascular Disease is now well organized and the chairmen of its sections on Clinical Cardiovascular Disease, Cardiovascular Surgery, Electrocardiography, Cardiovascular Physiology, Roentgenology, Pediatric Cardiology Therapy and Rehabilitation have begun work on their various projects We expect to receive many interesting reports on these projects at the annual meeting of the College in Atlantic City next June

"The committee also cooperates in presenting the cardiovascular sections in our various programs and postgraduate courses and, as a result, some outstanding panel discussions and lectures have been arranged during the past year"

Dr Bailey, chairman of the Section on Cardiovascular Surgery, reported that his section was conducting a study on cardiovascular surgery and that they hoped to report on this project at the annual meeting of the College in 1955

In the absence of Dr Paul H Holinger, Chicago, Chairman of the Committee on Audiovisual Aids, Dr Waterman, a member of the committee, presented the report The committee requested that its name be changed to "Committee on Motion Pictures" and that a separate Committee on Audiovisual Aids be appointed, inasmuch as its activities deal only with motion pictures Dr Jackson

moved that the recommendation be approved and that the President appoint a Committee on Audiovisual Aids to function on an equal footing with the Committee on Motion Pictures and that those who have shown special interest in this field be called upon to form the nucleus of this committee. The motion was seconded and approved. Dr Jackson suggested that the Committee on Audiovisual Aids not only should set up slide libraries, but also standards, qualifications, etc.

Mr Kornfeld reported on the following College books: **NONTUBERCULOUS DISEASES OF THE CHEST**. The publishers of this new book have reported that as of this date there has been a sale of approximately 1000 copies. This indicates that the book is enjoying a good sale and orders continue to arrive at the College office, as well as at the offices of the publishers. It was further reported that Spanish translation rights have been purchased by the Editorial Bibliografica Argentina, Buenos Aires, and the Spanish version of the book will go to press in the near future. The publishers have reported that there is a steady sale of the book entitled **THE FUNDAMENTALS OF PULMONARY TUBERCULOSIS AND ITS COMPLICATIONS**, companion to the new College book, which was published in 1949. Approximately 2500 copies of this book have been sold. Two new College books are now being prepared under the chairmanship of Dr Alfred Goldman, Los Angeles, and Dr Coleman B Rabin, New York City.

Dr Trimble, Chairman of the Board of Examiners, reported that 81 candidates were examined for Fellowship in the College at the annual meeting held in San Francisco in June of 1954, and that 16 candidates were examined at the Interim Session in Miami Beach on Saturday, November 27.

Dr McKay read the resolution concerning cancer of the lung which had been adopted by the Board of Regents at the San Francisco meeting. It was moved that the President appoint a committee of three to study the resolution and bring in a report at the next meeting of the Board concerning recommendations for changes or additions. The motion was seconded and approved.

Adjournment

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### COMMITTEE ON NOMINATIONS

Elections for offices expiring in June, 1955 will be held at the Ambassador Hotel, Atlantic City, June 4. Recommendations for elective offices may be addressed to the chairman of the Committee on Nominations, Dr Jay Arthur Myers, 1316 Mayo Memorial Building, University of Minnesota, Minneapolis 14, Minnesota. Other members of the committee are Dr Roy G Klepser, Washington, D C and Dr Howell S Randolph, Phoenix, Arizona.

### College News Notes

Dr Andrew L Banyai, Milwaukee, Wisconsin, Past-President of the College, will talk before the Oklahoma Academy of General Practice at its meeting in Oklahoma City on February 14 and 15. Dr Banyai will speak on "The Diagnosis and Treatment of Pulmonary Hemorrhage" and "Modern Treatment of Cough."

Dr James Alexander Lyon, Washington, D C, recently returned from a lecture tour which included Portugal, France, Italy, Ireland, and Spain. While in Spain, Dr Lyon presented a paper on "The Evaluation of Certain Arrhythmias" at the Third International Congress of the College and served on the panel discussing Cardiovascular Diseases.

Dr Irving Mack, Chicago, Illinois, was recently promoted to Clinical Assistant Professor of Medicine at the Chicago Medical School.

## College Fellows Honored

Dr Edgar Mayer, New York City, Regent of the College, was given the Cross of the Legion of Honor of France at a reception held in his honor at the French Consulate, New York City, on January 6. The Citation stated that "Dr Mayer, during World War I, effectively aided the United States Tuberculosis Commission to France through the medium of Dr Alexandre Bruno, who acted as intermediary agent between the Commission and the French people. The work of this Commission led to the development of the French Saranac at Passy to which for years Dr Mayer served in a consultant capacity and was a frequent lecturer there. Since then, Dr Mayer has been a lecturer on occasion at the Laennec Hospital and the Hospital Boucicourt in Paris, and has aided in the publication of French contributions to medicine in American journals. He is also actively engaged in the creation of a Memorial Fund at the French Saranac in Passy to commemorate the work of the American Tuberculosis Commission that served during World War I, as well as in the interchange of medical lectures between the United States and France."

Dr Chevalier L Jackson, Philadelphia, Pennsylvania, Past-President of the College, was the recipient of the First Citizens Committee Award of the Philadelphia Civic Grand Opera Company at a dinner given in his honor at the Bellevue Stratford Hotel on December 20. The citation read as follows: "On this, the occasion of your twenty-fifth year of Humanitarian and Civic Service, we, your friends and colleagues, are privileged to honor you for your illustrious record of service. We give public expression to the esteem and affection in which you are held, not only by those who have benefited directly by your efforts, but by all who know your undeviating devotion to the highest American ideals, to truth in science, and in the arts, and to service to your fellow-man. We salute you as a brilliant leader in the field of medicine, as a loyal friend, as an outstanding humanitarian and an inspiring patron of the arts."

Dr William C Voorsanger, senior physician on the medical staff at Mount Zion Hospital, San Francisco, was awarded a certificate of merit at the hospital's annual meeting held recently in recognition of his fifty years of service there. Dr Voorsanger was a pioneer worker in the battle against tuberculosis and, in 1905, assisted in the founding of the medical staff of the hospital; he has served on its staff since then. In recognition of Dr Voorsanger's contributions to the hospital for over half a century, it was announced that the William C Voorsanger Fund has been created to further the investigation of pulmonary diseases. During his career, Dr Voorsanger has been chief of medical services and head of the chest service and tuberculosis clinic at the hospital. In addition he is a founder and past president of the California Tuberculosis Association and past president of the San Francisco Medical Society.

Dr Alton Ochsner, New Orleans, Louisiana, Dr Myron Prinzmetal, Los Angeles, California, Fellows of the College, and Dr Selman A Waksman, New Brunswick, New Jersey, a recipient of the College Medal for outstanding achievement in diseases of the chest, were among the ten scientists honored by "Modern Medicine" for distinguished achievement in medicine.

Professor Ludwig Heilmeyer, Governor of the College for Freiburg, Germany, was awarded the Carlos Finlay Medal of Cuba for distinguished contributions to medical science.

# College Chapter News

## CALIFORNIA CHAPTER

The annual meeting of the California Chapter will be held at the Palace Hotel, San Francisco, April 30, 1955, immediately preceding the meeting of the California Medical Association, May 1-5

Out-of-town speakers who wish to submit papers for presentation at the chapter meeting are requested to communicate with Dr Marvin S Harris, Secretary, 6317 Wilshire Boulevard, Los Angeles, California

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## CUBAN CHAPTER MEETING

A meeting of the Cuban Chapter of the College was held at the Hospital Curie in Havana on Wednesday, December 1, 1954. Forty-two members of the College and their wives who had attended the Interim Session of the College in Miami Beach, flew to Havana on Tuesday, November 30, to participate in the meeting. A friendly welcome was accorded the College group upon their arrival at the Havana airport, by the officials of the chapter. A bus was waiting at the airport to take the group to the Hotel Nacional.

The Cuban Medical Association gave a reception and luncheon for the group on Wednesday, December 1, at the headquarters building of the Association. The presidents of both the Cuban and the Havana Medical Associations were present and welcomed the College members in a brief ceremony held in the private auditorium of the Association. The President of the College, Dr William A Hudson, responded with an expression of sincere appreciation of the cordial hospitality extended to the College visitors by their Cuban colleagues. After lunch, a bus was waiting to take the group on a tour of Havana. A cocktail party was also given for the College members at the Bacardi Bar in downtown Havana. The scientific session was held that evening at the Hospital Curie.

Dr Antonio Navarrete of Havana, Regent of the College for Cuba, and the other officials of the Cuban Chapter, Dr Teodosio Valledor, Governor, Dr H Anido Fraguio, President, and Dr Antonio Rodriguez Diaz, past-president, deserve the highest praise for arranging a splendid program for the College members from the United States, who will long remember their enjoyable visit to Havana. A special vote of thanks was extended to Dr Manuel Conde, a Fellow of the College and President of the Cuban Medical Association, for their hospitality.

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## PENNSYLVANIA CHAPTER

The Pennsylvania Chapter will present a diagnostic x-ray conference on Monday evening, March 7, at the Bellevue-Stratford Hotel, Philadelphia, following the banquet of the 8th Annual Philadelphia Postgraduate Course on Diseases of the Chest, which will be held March 7-11.

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## ANNOUNCEMENTS

Groningen University (Holland) will sponsor its Fifth Postgraduate Course of Thoracic Clinical Science and Surgery, May 23-June 13, 1955. The World Health Organization has invited its member states to send participants to the course and has allocated funds for their individual fellowship donations. Prof L D Eerland, Regent of the College for Holland, is Chairman of the course and Prof R Brinkman is Secretary.

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The annual meeting of the Aero Medical Association, under the Presidency of Brigadier General Otis O Benson, Jr, will be held at the Hotel Statler, Washington, D C, March 21-23, 1955.

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The Los Angeles County Tuberculosis and Health Association and the Los Angeles Trudeau Society will sponsor the 5th Pulmonary Diseases Symposium February 4, 5, 6, 1955.

# Obituary

## MAZZINI BUENO

1889-1954



The world has just lost a teacher, author and pioneer in the field of tuberculosis. Unusual ability, a straightforward manner, and a dedication to the sick, combined with kindness and a cheerful heart, made Dr. Bueno a great physician. He graduated from the University of Brazil—then the University of Rio de Janeiro—in December, 1910. He interned at Santa Casa de Misericórdia in the same city. He was appointed Assistant Professor of Medicine and served under the great Brazilian physician, Miguel Pereira, from 1911 to 1917. As early as 1914, he instituted pneumothorax therapy, the first of such treatment to be given in a medical school and community hospital in Brazil. In 1923, he was co-founder and Professor of Medical Diagnosis and Tuberculosis in the Fluminense Medical School of the University of the State of Rio de Janeiro. He was the first Brazilian physician to be placed in charge

of a pavillion for tuberculosis patients. This was in the Hospital Sao Sebastiao, Rio de Janeiro, in 1918. In 1922, the Brazilian Department of Public Health asked him to take charge of pneumothorax therapy. While associated with that department, he had great influence over many physicians who were then prominent in this field in Brazil. Dr. Ary Miranda, Dr. Genesio Pitanga, Dr. Alberto Renzo and the late Dr. Alexander Stockler. Dr. Bueno was a contemporary of Dr. Manuel de Abreu and gave support to this important and world-renowned work on photoroentgenography.

In 1924, Dr. Bueno published his first book concerning collapse therapy. In addition to the books he wrote on diseases of the chest, Dr. Bueno published several scientific treatises. One important paper entitled, "Changes of Volume of Pulmonary Cavities Due to Bronchial Disturbances," was published in 1932. Dr. Bueno was a co-founder of the Brazilian Tuberculosis Society. His associate members recognized his great contributions by electing him as President, both of this Society and the Central Brazilian Chapter of the American College of Chest Physicians.

Over one thousand people attended his Mass—a traditional ceremony in Brazil. His wife, Laura, and six children, including two physicians—Marcio and Roberto—survive him.

The memory of Dr. Bueno will be perpetuated forever by his writings and in the good works of many dedicated students.

RICHARD H. OVERHOLT, M.D.

# DISEASES of the CHEST

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## Typical and Atypical Electrocardiograms in Myocardial Infarction Caused by Acute Coronary Occlusion and Coronary Insufficiency\*

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New York, New York

Acute coronary episodes vary a great deal in severity and pathologically.<sup>1,5</sup> On the one hand there are attacks of intense, prolonged pain beginning at rest, accompanied by a drop in blood pressure, gallop rhythm, shock or congestive failure which almost always indicate a coronary occlusion with massive infarction. At the other end of the scale are the mild episodes in which the pain is of short duration and in which there are no changes in cardiac function and blood pressure. These attacks are usually caused by coronary insufficiency with either ischemia or necrosis of the subendocardial area. However, not infrequently coronary occlusion with major infarction also produces mild symptoms or the acute attack is preceded by one or more attacks of pain indistinguishable from coronary insufficiency.<sup>3,6,9</sup> The differential diagnosis depends largely on the electrocardiographic findings. In over 90 per cent of cases, because they result in different types of infarction, coronary occlusion and insufficiency produce characteristic electrocardiographic patterns. As might be expected, there are numerous atypical changes, particularly as the coronary occlusion is forming and finally causes complete obstruction.

### *Typical Changes*

*Acute Coronary Insufficiency* Mild degrees of coronary insufficiency produce subendocardial ischemia, more severe forms cause focal necrosis or infarction of the subendocardial layer.<sup>1-4</sup> Since the ischemia or necrosis is disseminated, the electrocardiogram shows RS-T depressions and/or T-wave inversions in several or all leads. In subendocardial ischemia, the changes in the electrocardiogram revert to normal within hours or several days. In subendocardial necrosis, they persist for several weeks, months, or at times, longer.

The following two cases illustrate this difference.

*Case 1* A S., a 48-year-old business executive, suddenly experienced precordial pain and an electrocardiogram one hour later showed slight ST depression in V<sub>3</sub> (Fig 1). Several minutes later the pain recurred and the depression in this lead increased. Two days later the electrocardiogram showed changes in the T-wave in leads I and V<sub>3-6</sub>. The physical examination, blood pressure, temperature and sedimentation rate were normal and remained so. On the eighth day the electrocardiogram had returned

\*From the Cardiographic Laboratory, The Mount Sinai Hospital, New York

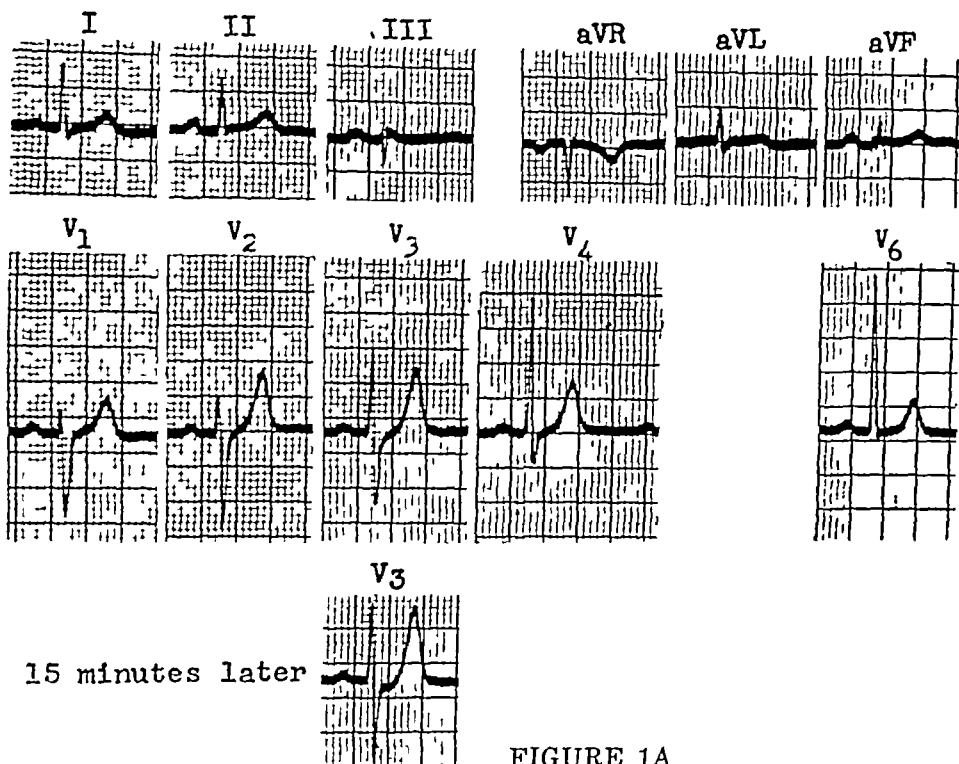


FIGURE 1A

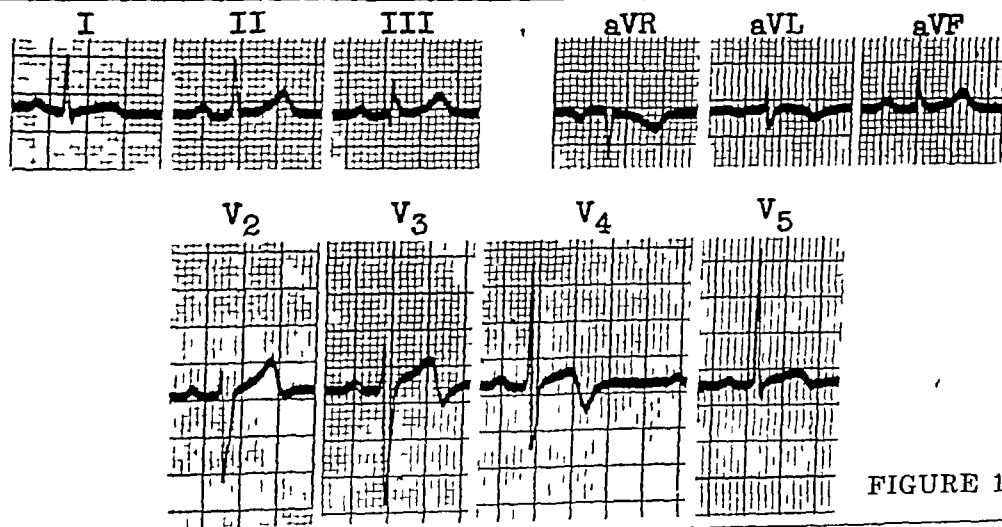


FIGURE 1B

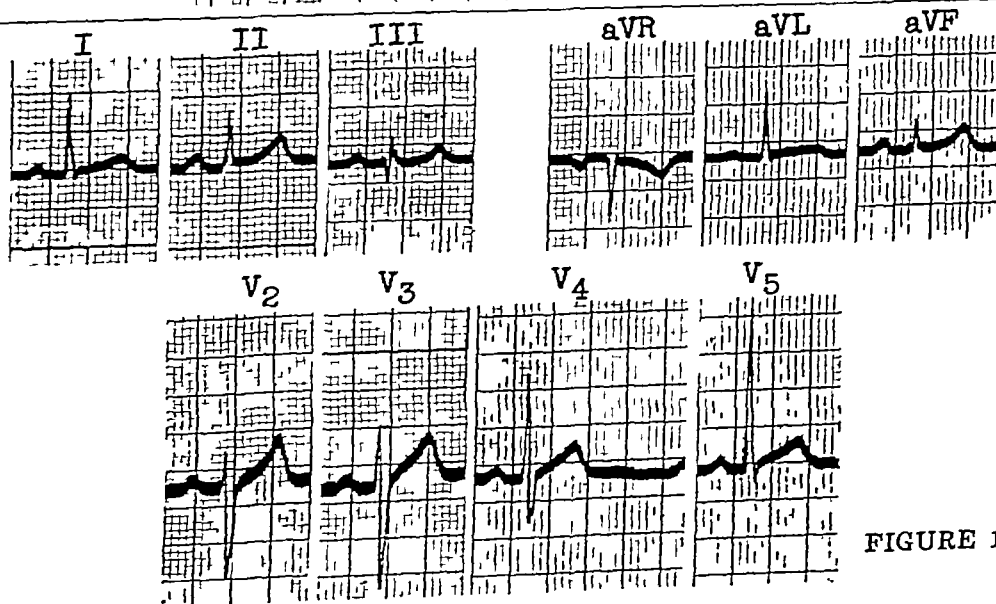


FIGURE 1C

← (At Left)

**FIGURE 1A** A S, m, 48 Acute coronary insufficiency One hour after attack minimal ST depression present in V<sub>5</sub>. This depression increased during recurrence of pain—**FIGURE 1B** A S, m, 48 Acute coronary insufficiency Record taken 2 days after acute attack Temperature and sedimentation rate normal—**FIGURE 1C** A S, m, 48 Eighth day, record normal

to normal He was permitted out of bed in one week and has been well during the two years which have elapsed since the attack

The failure of the heart sounds, blood pressure, temperature or sedimentation rate to change stamps this as a case of coronary insufficiency with subendocardial ischemia, without significant necrosis

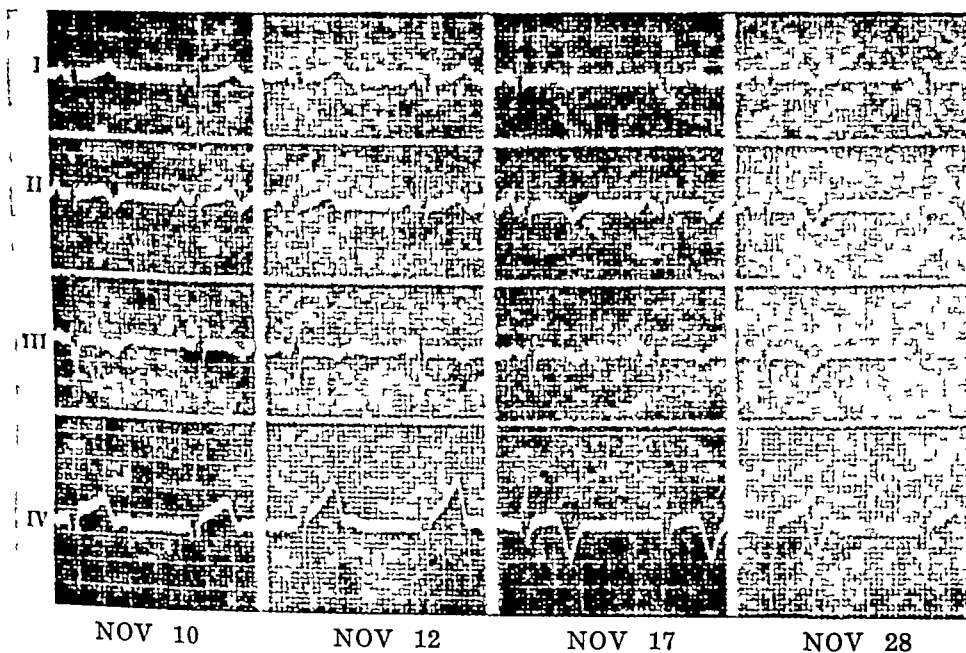
**Case 2** R E, an athletics teacher, developed precordial pain for the first time at 37 It lasted two hours, after which he felt "swell" He visited the clinic on the third day and an electrocardiogram showed T-wave inversion in leads II and III (Fig 2) His temperature was 101° and his W B C was 14,000, indicating subendocardial necrosis Two days later the electrocardiogram was within normal limits but on the ninth day of the attack it showed inversion of the T-wave in all leads which progressed during the next 11 days His course was uneventful

Although clinically mild, this was a definite case of subendocardial infarction with persistent T-wave inversion

In some of these cases the T-wave changes may not appear for one or two weeks after the clinical attack, even though the sedimentation rate had become normal after several days

Since infarction secondary to coronary insufficiency is usually not extensive, the prognosis is excellent as a rule In other words, when the electrocardiogram shows only T-wave inversions, the patient almost always recovers<sup>10</sup>

Occasionally coronary insufficiency produces temporary RS-T elevation instead of depression, thus at first simulating acute coronary occlusion with major infarction<sup>11</sup> This is true, particularly, of the precordial leads in



**FIGURE 2** E R, male, 37 November 10—sinus bradycardia, rate 60 beats per minute. Left axis deviation T-II diphasic, T-III inverted November 12—T-II now upright, T-III only slightly inverted November 17—T-I diphasic, T-II, T-III, and T-IV inverted November 28—T-waves definitely inverted in all leads, indicating myocardial infarction—From Jaffe, Master and Kalter, *New York State Journal of Medicine*, 1945



patients with previous anterior infarction, for example, if such a patient develops tachycardia, spontaneously or after exertion, the electrocardiogram may present distinct RS-T elevation, in addition to the chronic Q-wave. As soon as the tachycardia remits, the RS-T elevation disappears.

*Coronary Occlusion* Characteristically, coronary occlusion produces a

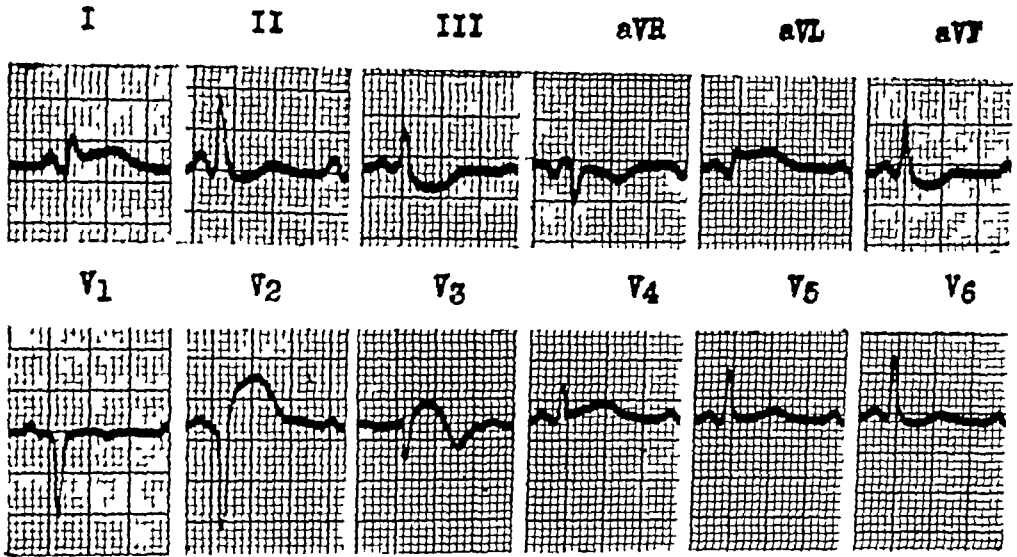


FIGURE 3A

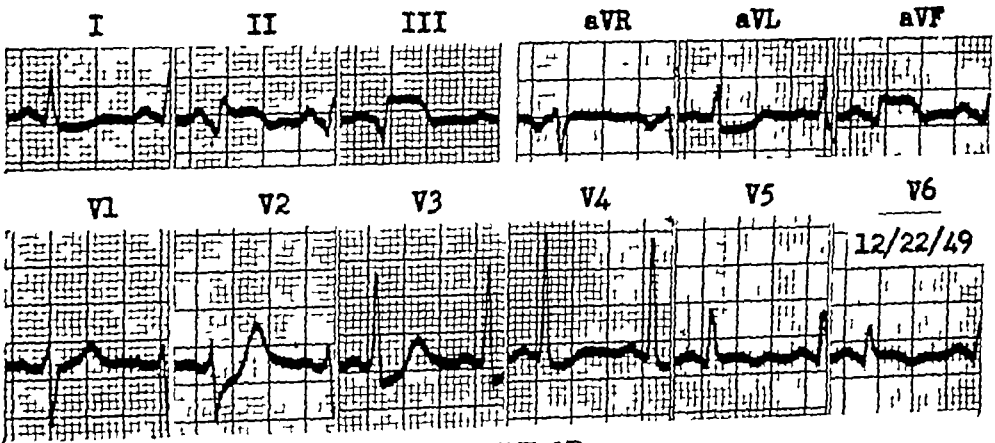
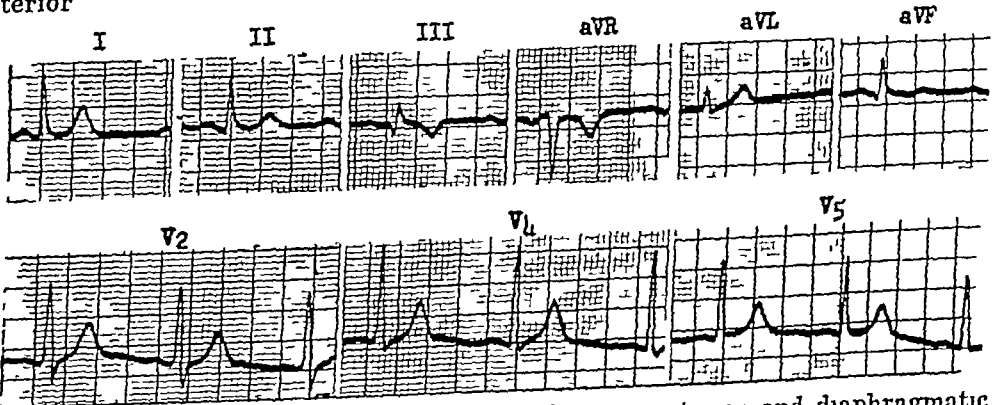


FIGURE 3B

*Figure 3A* A M, m, 53 Acute coronary occlusion Q-waves in I, aVL, V<sub>1-3</sub> with corresponding RS-T elevations *Figure 3B* J S, m 58 Acute coronary occlusion Posterior



*FIGURE 4* G B, m, 34 Acute coronary occlusion, posterior and diaphragmatic infarction A Q-wave and T-wave inversion developed in lead III but not in aVF. Note the tall R in V<sub>2</sub>.

massive, through and through infarct and the electrocardiogram presents RS-T elevations and Q-waves (Fig 3) The time of appearance of these changes is variable In occasional cases the electrocardiogram remains

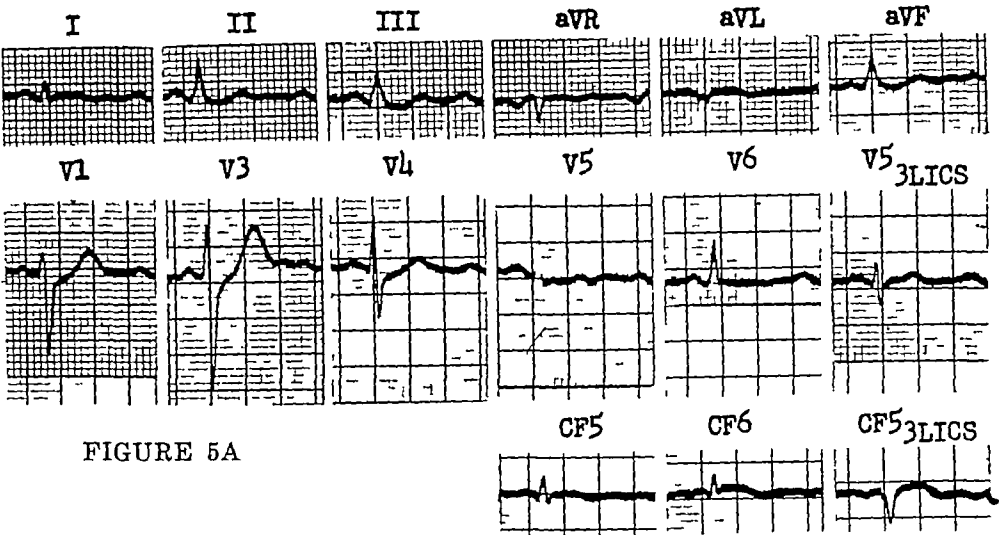


FIGURE 5A

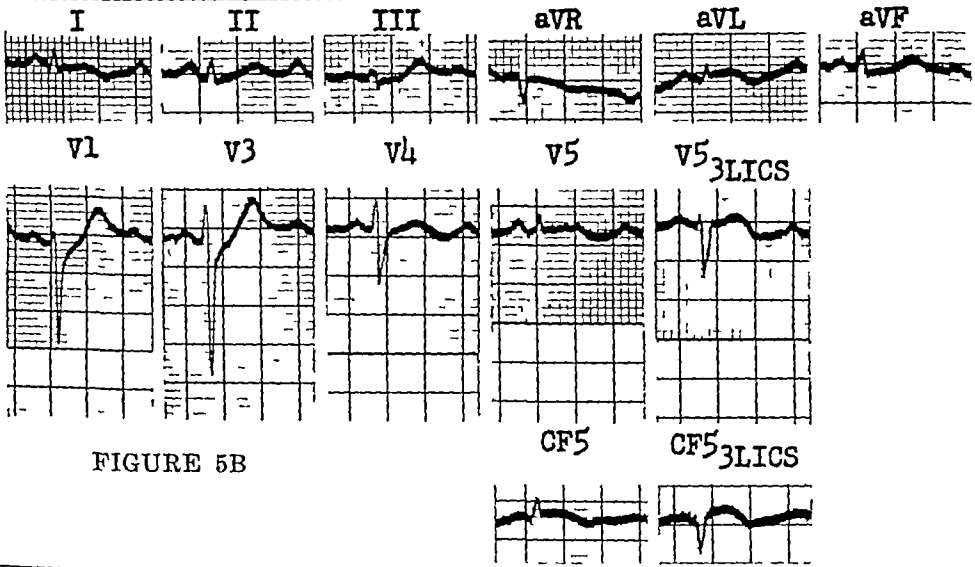


FIGURE 5B

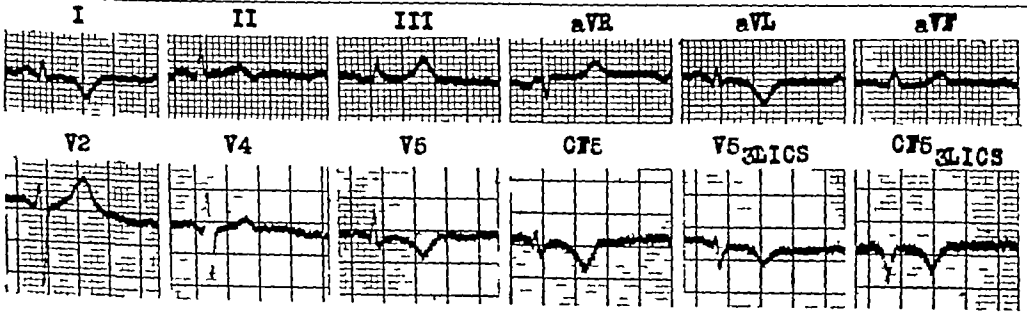


FIGURE 5C

Figure 5A L W, m 64 Coronary occlusion with high lateral wall infarction, shown by CF and aVL leads but not by V leads Record taken 10 hours after onset.—  
Figure 5B L W, m, 64 Coronary occlusion with high lateral infarction, Q-wave present in aVL and CF but not in V leads Record taken 30 hours after onset—  
Figure 5C L W, m, 64 Coronary occlusion with high lateral wall infarction Two weeks after onset

normal or unchanged for six to 10 hours, in spite of severe, persistent pain. Rarely both RS-T elevation and Q-waves appear within an hour or two after the acute attack. In many cases in which an electrocardiogram is taken within several hours, only marked RS-T elevation is present and the Q-waves do not appear until 12 to 20 hours later.

In which leads these changes appear depends upon the site and extent of the infarct. If the anterior surface of the left ventricle is infarcted, the Q-waves and RS-T elevations appear in leads 1, aVL and the precordial leads (Fig 3A). In diaphragmatic (usually termed posterior) infarction, leads 3 and aVF show these changes (Fig 3B), although in some cases the Q-wave appears in lead 3 and not in lead aVF (Fig 4). An anterior infarct may be localized to the septal area, in which case the Q and RS-T elevations appear only in  $V_1$  to  $V_{3,4}$ , or to the lateral surface, in which case these changes are usually present only in leads 1, aVL and  $V_{5,6}$  or at times only in leads 1 and aVL. In some cases it is necessary to take special precordial leads other than  $V_1$  to 6 in order to obtain the characteristic changes. This is illustrated in Fig 5. The patient, a merchant of 58, developed moderately severe substernal pain and a record taken 10 hours later showed only slight RS-T and T-wave changes in the routine unipolar chest leads and in those taken in the third left interspace. However, CF leads in the routine positions showed RS-T elevation and in the third interspace a large Q-wave as well. In this case, the optimum chest lead was CF and the best position the third interspace. Of course, characteristic changes were present in aVL from the start.

Frequently, the infarction extends from one surface of the left ventricle on to another and the typical Q-waves and RS-T elevations appear in various combinations of leads, e g, in an infarct involving the diaphragmatic and antero-septal surfaces, they occur in leads 3, aVF and  $V_1$  to 3. Involvement of several areas is much more common than has usually been stated and results in considerable variation of the electrocardiographic patterns in coronary occlusion.

In coronary occlusion the electrocardiogram frequently shows reciprocal RS-T and T changes in various leads, e g, between leads 1 and 3, aVL and aVF and, occasionally, between  $V_{1,2}$  and  $V_{5,6}$  (Fig 3). This reciprocal relationship is obscured when pericarditis is present or when both the anterior and diaphragmatic surfaces are infarcted.

During the acute stage of infarction, the RS-T and T-waves show progressive, serial changes. The RS-T elevation gradually diminishes and disappears after two to four weeks (unless a ventricular aneurysm forms) and the T-wave becomes increasingly inverted for three to six weeks. The Q-wave usually shows little alteration during the acute stage although, occasionally, it disappears within a month or two.

In our experience, prognosis during the acute stage of coronary occlusion is not determined by the magnitude of the electrocardiographic changes. Many patients with large Q-waves and deeply inverted T-waves in all chest positions, and even some with persistent RS-T elevation for a number of weeks, run a benign course and become ambulatory in the

usual three or four weeks. Similarly, we have not found the sedimentation rate an accurate index of the severity of the attack.

### *Atypical Electrocardiograms*

As might be expected, there are exceptions to these rules. In 5 to 10 per cent of cases coronary insufficiency produces a large infarct with RS-T elevation and Q-waves, whereas coronary occlusion produces an intramural (rather than a through and through) infarct and the electrocardiogram shows only T-wave abnormalities. An atypical electrocardio-

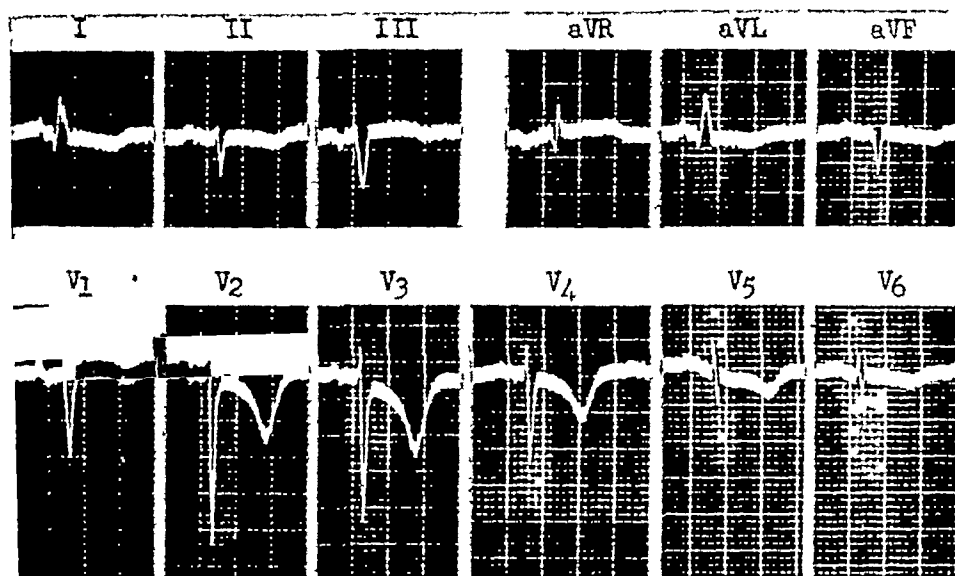


FIGURE 6A

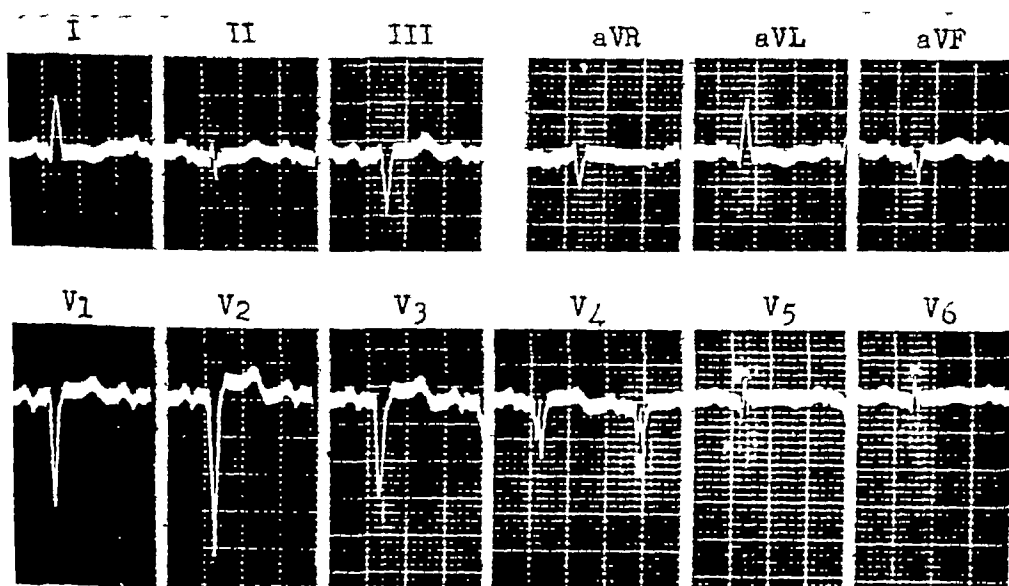


FIGURE 6B

Figure 6A R K, f, 60. Premonitory phase of coronary occlusion. Precordial pain for 2½ days. Temperature, 99.6, WBC 22,000, Polys 82 per cent. Record shows RS-T depressions and T-wave inversions.—Figure 6B R K, f, 60. Acute coronary occlusion with antero-septal infarction after 8 days of precordial pain. Temperature, 100. Q-waves and RS-T elevations now present in chest leads.

gram is also found in infarction of the true posterior surface (as opposed to diaphragmatic infarction which is ordinarily termed "posterior") In such infarction a tall R-wave and tall T-waves are often present in  $V_1, 2$  and in later stages the tall R-wave may be the only indication of previous infarction (Fig 4) <sup>12 13</sup> To be sure, a tall R-wave in  $V_1$  is often seen as part of the typical pattern of a massive antero-lateral infarct and it must also be remembered that such an R-wave is present occasionally in normal persons and frequently in right ventricular enlargement

*The Premonitory Phase of Coronary Occlusion* Another difficulty in immediately diagnosing the exact nature of acute coronary episodes results from the fact that coronary occlusion with major infarction is often preceded by an attack of pain or recurrent anginal pain at rest or on effort over a period of days or weeks <sup>1 6 9</sup> During this period the electrocardiogram may be normal or remain unchanged, but usually it shows the changes of coronary insufficiency, i e, RS-T depression and/or T-wave inversion (Fig 6) In other words, many cases of coronary occlusion begin as acute coronary insufficiency, with subendocardial ischemia or necrosis, and at the onset are indistinguishable from the two cases outlined above However, after a number of days or weeks, the patient develops a more acute attack and Q-waves and RS-T elevations appear on the electrocardiogram Occasionally, however, these changes appear without an acute attack or even when the pain has subsided It should be emphasized that the majority of cases of acute coronary insufficiency which fit the description of impending coronary occlusion gradually subside without going on to a major infarction

In a few cases the coronary insufficiency changes, i e, RS-T depression and/or T-wave inversion, persist for a day after the coronary occlusion attack has occurred, before being succeeded by RS-T elevation and Q-waves Occasionally such changes are present temporarily after the acute occlusion even when there has been no premonitory stage (Fig 7)

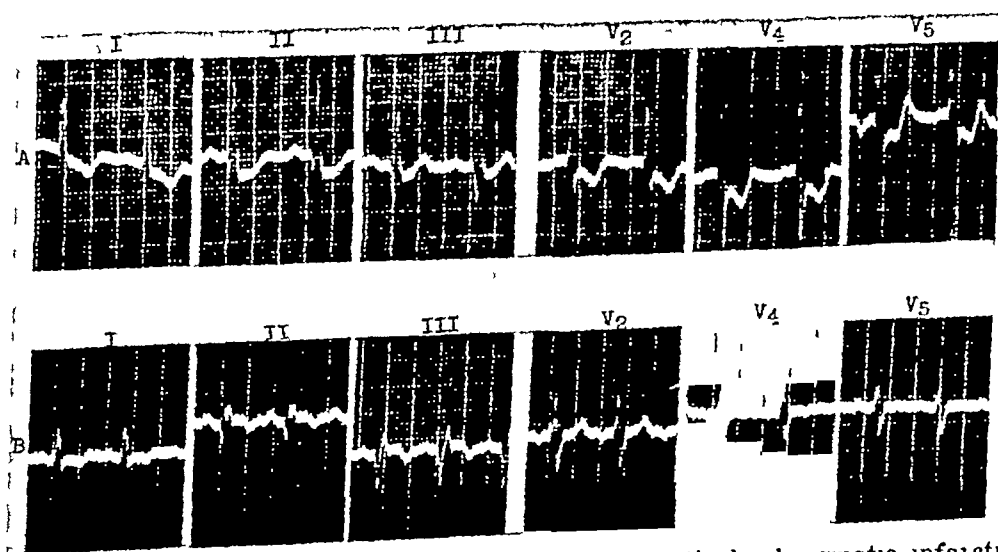


FIGURE 7 L F, m, 63 Acute coronary occlusion with diaphragmatic infarction Angina pectoris for eight years with probable previous infarction A One hour after acute attack of pain B Twelve hours later

Another type of electrocardiographic change occasionally encountered at the very onset of coronary occlusion, i e, very tall T-waves,<sup>14</sup> is shown in Fig 9 This record was taken within one hour after the onset of severe pain in the mid-back At this time the RS-T segments were still depressed In some cases this type of T-wave persists for some hours until the RS-T has become elevated but usually the T has diminished in size by this time or by the time Q-waves have appeared

*Temporary Improvement of Electrocardiogram* A number of years ago we pointed out that in myocardial infarction RS-T and T-wave changes may temporarily improve between the third and tenth day after the attack, and the electrocardiogram may appear normal<sup>10 15</sup> At that time we considered this an unusual occurrence, but since then we have observed it more frequently It is our impression that it occurs in approximately 5 per cent of cases This finding is of some practical importance

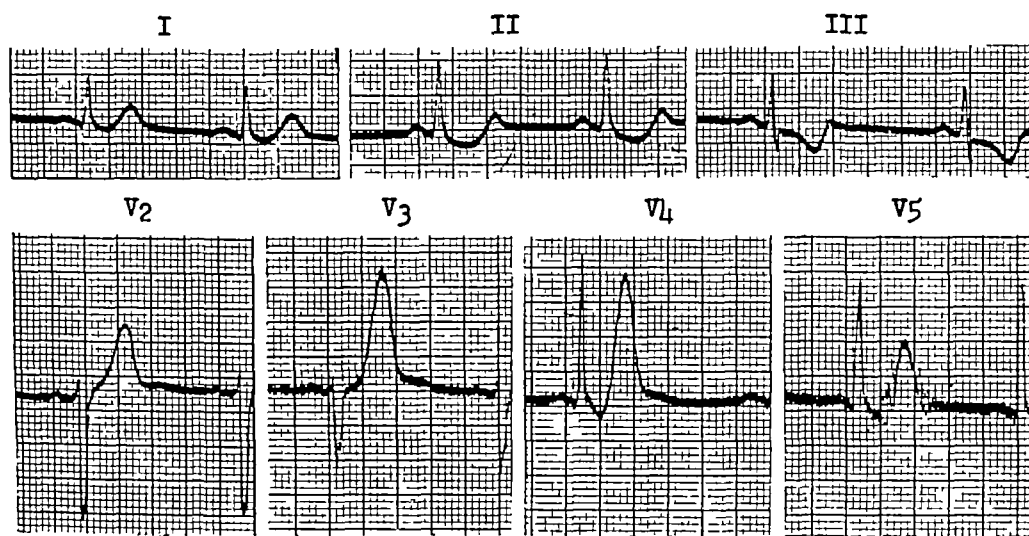


FIGURE 8A

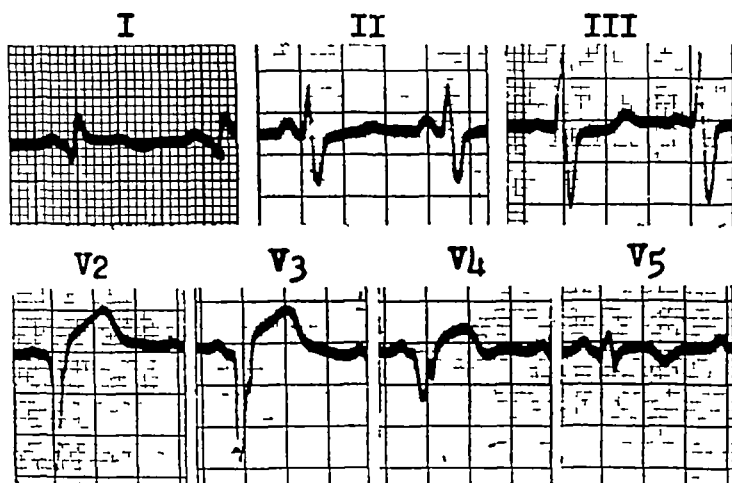


FIGURE 8B

Figure 8A H S, m, 51 Coronary occlusion One hour after the onset of severe posterior chest pain No previous symptoms—Figure 8B H S, m, 51 Coronary occlusion with antero-septal infarction, fifth day

for two reasons. The first electrocardiogram may not be taken until after the third day of the attack, if it is temporarily normal, the correct diagnosis may be missed. Secondly, the temporary improvement in the electrocardiogram may lead the physician to permit the patient to become active prematurely. Therefore, when the electrocardiogram improves rapidly following a coronary episode, this should be confirmed in several records.

Temporary return of the electrocardiogram to normal is illustrated in Fig. 2 and the case history has been outlined. The mechanism of this electrocardiographic finding is not clear. Such a change, i.e., an inverted T-wave becoming upright, may signify extension of the myocardial ischemia or necrosis, but in our cases there has been nothing in the clinical course to indicate this. From a similar point of view, it has been suggested that the electrocardiographic "improvement" occurs at the time when the blood pressure has fallen considerably, resulting in coronary ischemia. This, too, did not seem to be a significant factor in our cases. For example, in the case cited, the blood pressure was 130/96 at the time the electrocardiogram returned to normal, and fell moderately only several days later. Pericarditis has also been suggested as an explanation for the temporary improvement<sup>10</sup> but this would not account for transitory disappearance of RS-T elevation which we have observed in some cases.

#### *Comment*

We have indicated some of the changes in the ECG encountered in acute coronary episodes. The most interesting cases are the mild or moderately severe attacks with only RS-T depressions and/or T-wave inversions in the ECG. This type of attack may follow one of these courses: 1) The ECG returns to normal (or to its previous pattern) in a few days and there is no laboratory evidence of infarction or necrosis, i.e., the temperature and sedimentation rate remain normal. In these cases the pain and temporary ECG changes are the result of subendocardial ischemia. 2) The ECG changes persist for several weeks or months and there is some fever and elevation of the sedimentation rate during this period. In these cases subendocardial necrosis is present and the outlook is excellent. 3) The patient continues to experience recurrent pain during which the RS-T depression and T-wave changes may vary considerably and the sedimentation rate may be elevated. After a period of hours, days or weeks a severe attack develops, indicating coronary occlusion. The RS-T depression present during the premonitory phase may persist during the day after the occlusion, or very tall T-waves may appear temporarily. This is usually followed by marked RS-T elevation and, later, by Q-waves, the typical findings in massive infarction.

The last group of cases emphasize the fact that it often takes days or weeks for a thrombus to cause complete obstruction of a coronary artery. As the thrombosis becomes complete, we have seen how the electrocardiogram may show various quickly changing patterns. There is some difference of opinion as to how the process of coronary thrombosis is initiated. Some authors believe that usually it does not start directly on a sclerotic plaque but is secondary to a subintimal hemorrhage which has resulted in

injury to the intima.<sup>3</sup> Such a hemorrhage may also result in a hematoma which obstructs the lumen.

These subintimal hemorrhages are a common occurrence in sclerotic arteries and may cause diminution in the coronary flow, i. e., coronary insufficiency, without producing changes in the intima or thrombosis. This is probably the underlying mechanism in many of the cases in Groups 1 and 2 with ST depression and/or T-wave changes. However, many cases in these groups, particularly in Group 1 in which the electrocardiographic changes are transitory, are probably instances of coronary insufficiency precipitated by physical and emotional strain. And in some of the cases in Group 2, with persistent T-wave inversion, a coronary thrombosis with localized infarction is probably present. Because the infarct is not extensive, there are no Q-waves or RS-T elevations.

#### SUMMARY

When an acute coronary episode occurs, if the initial electrocardiogram does not indicate a coronary occlusion, it may be difficult at first to determine the exact nature of the attack. The electrocardiogram may remain normal for a variable period or may indicate coronary insufficiency and myocardial ischemia. In the cases going on to coronary thrombosis and massive infarction, the electrocardiogram may show various rapidly changing patterns before the appearance of RS-T elevation and Q-waves. In coronary occlusion the electrocardiogram often shows involvement of more than one surface and variations of the typical patterns are frequent. The changes may be present in only a few of the 12 routine leads or only in special chest positions.

In an acute coronary episode it is essential to keep the patient at rest until the extent of myocardial involvement has been determined.

Not infrequently the electrocardiogram shows temporary improvement or actual return of RS-T and T to normal between the third and 10th days following myocardial infarction.

#### RESUMEN

Cuando ocurre un episodio coronario agudo, si el electrocardiograma no indica una oclusión coronaria, ser difícil al principio el sentar un diagnóstico. El electrocardiograma puede permanecer normal por un período variable o puede indicar insuficiencia coronaria e isquemia del miocardio. En los casos que marchan hacia la trombosis coronaria y el infarto masivo, el electro puede mostrar varios aspectos rápidamente cambiantes antes de la elevación RS-T aparezca así como las ondas Q.

En la oclusión coronaria el electro a menudo muestra compromiso de más de una superficie y las variaciones del aspecto típico son frecuentes.

Los cambios pueden presentarse en sólo pocos de los doce puntos de rutina o sólo en posiciones especiales del tórax.

En un episodio agudo coronario es esencial conservar al enfermo en reposo hasta que la extensión del daño miocárdico se haya determinado.

No es poco frecuente que el electrocardiograma muestre una mejoría temporal o verdadero regreso de RS-T y T a la normal el tercero y el décimo día después del infarto del miocardio.



## RESUME

Lors d'un épisode coronarien aigu, si l'électrocardiogramme n'indique pas dès le début l'existence d'une occlusion coronarienne, il peut être difficile de déterminer la nature exacte d'une telle attaque. L'électrocardiogramme peut rester normal pendant un période de temps variable ou peut indiquer une insuffisance coronarienne avec ischémie myocardique. Dans les cas où l'évolution se fait vers la thrombose coronarienne et l'infarctus massif, l'électrocardiogramme peut montrer des aspects variés et rapidement changeants, avant que n'apparaisse l'élévation de R S T et de l'onde Q. Dans l'occlusion coronarienne, l'électrocardiogramme montre souvent des altérations de plusieurs parois et les variations du dessin classique sont fréquentes. Les altérations peuvent n'exister que sur un petit nombre des douze dérivations classiques ou bien uniquement dans le cas de position particulière du thorax.

Lors d'un épisode aigu, il est essentiel de laisser le malade au repos jusqu'à ce que soit déterminée l'étendue des lésions myocardiques.

Il n'est pas exceptionnel de constater à l'électrocardiogramme une amélioration ou bien un retour à la normale des ondes R S T et Q entre le troisième et le dixième jour suivant la constitution de l'infarctus myocardique.

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# Cardiac Diagnostic Methods in Coronary Artery Disease: Electrocardiogram, "2-Step" Exercise Test and Ballistocardiogram

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The clinical importance and necessity of dependable cardiac diagnostic and function tests are emphasized by the outstanding fact that cardiovascular disease is the leading cause of death in the country today. However, the time honored methods of complete history, adequate physical examination, chest fluoroscopy and roentgenogram will never be replaced in value by the other available tests of heart function. The latter serve as corroborative laboratory aids for diagnosis and prognosis and in this regard, they play a vital role in the final clinical impression of the cardiac status.

## *Electrocardiography*

Since the introduction of an accurate recording apparatus, the electrocardiograph has assumed increasing importance daily in the routine diagnosis of coronary artery disease.

*Technique* Although the present electrocardiographic recording apparatuses leave much to be desired insofar as high frequency response is concerned, the customary amplifier type or string galvanometers yield records of sufficient fidelity for routine clinical use. All records should be accompanied by the standardization utilized, that is, 1 milli-Volt = 1 centimeter deflection for routine tracings. At present 12 lead records are recommended routinely: the three standard leads (I, II and III), the three augmented unipolar limb leads (aVR, aVL and aVF), and the six unipolar precordial chest leads (V<sub>1</sub> through V<sub>6</sub>). Although less than the 12 mentioned are recorded routinely in many cardiac laboratories, instances of coronary disease in which abnormalities occur in only one lead are sufficiently common to preclude such abbreviations of technique. Moreover, situations such as high lateral myocardial infarction, may require even additional chest exploration for the detection of the cardiographic alteration.

The use of CR, CL or CF chest leads routinely as opposed to unipolar V leads introduces the valid objection of undue influence of the remote extremity electrode on the exploring chest piece. Current argument in favor of CF over V chest leads cannot be supported on theoretical grounds and any diagnostic advantage in an individual case may be considered merely fortuitous. On the other hand, the apparent advantage of unipolar extremity leads such as aVF in the diagnosis of posterior (diaphragmatic) myocardial infarction has been questioned by many workers.

Somatic tremor may usually be readily eliminated, but in some cases, as in Parkinsonism, may produce a regular undulation of the baseline.

which may be mistaken for auricular flutter Alternating current interference should be eliminated by proper grounding

*Interpretation* The criteria for normality and abnormality of electrocardiographic tracings as regards coronary artery disease are generally universally accepted, although individual interpretations may vary Unfortunately, normal individuals as well as those with anxiety states may present abnormal resting electrocardiographic tracings Ergotamine<sup>1</sup> and more recently, dihydroergocornine,<sup>2</sup> have been utilized in the differentiation of such abnormal resting electrocardiographic tracings in functional heart disturbance as compared with organic coronary artery disease, the record returning to normal during exhibition of these drugs in the former condition

Interpretation of electrocardiographic records as regards coronary disease without adequate knowledge of the age and clinical status of the patient is fraught with danger Refusal to render a reading of tracings without this information is actually entirely justifiable For example, the cardiac rotation and displacement with pulmonary collapse may result in electrocardiographic "abnormalities" in the absence of cardiac involvement

*Specificity* The Q waves of myocardial infarction represent the truly specific alterations of the electrocardiogram diagnostic of complete coronary artery occlusion Although the appearance of significant Q waves may be delayed for several days or longer after acute coronary occlusion with through and through myocardial infarction, they usually remain permanently as the indicator of previous severe myocardial damage With subsequent episodes of acute coronary occlusion, Q waves may appear in other leads or become deeper and/or wider, if already present Q waves are usually considered significant only when they represent 25 per cent or more of the amplitude of the R wave or when they are 0.04 second or longer in duration It should be remembered that a deep Q or QS deflection is a normal finding in lead aVR and that myocardial infarction may be reflected in this lead by the appearance of an early R wave<sup>1</sup> Even in the absence of significant Q waves, anterior wall myocardial infarction may be diagnosed by an alteration of the normal increment of the amplitude of the R wave as one proceeds from V<sub>1</sub> through to lead V<sub>6</sub> on the chest wall In some instances, after recovery from acute coronary occlusion, the Q waves may become smaller and some records may lose the Q wave entirely and become normal

RS-T segment deviations and T wave alterations are *not* specific for coronary artery disease Unfortunately, these abnormalities may be associated with many other disease states such as rheumatic heart disease, pericarditis of any etiology, cardiac hypertrophy of any cause, pulmonary embolization, etc Moreover, electrolyte imbalance (potassium, calcium) and even drinking of ice water may produce electrocardiographic changes in the RS-T segment and/or T waves indistinguishable from those associated with organic coronary artery disease It is important to emphasize the difference between the electrocardiographic pattern of acute coronary

insufficiency and that of acute coronary occlusion. In the former there is noted typically RS-T segment depression and T wave inversion in all leads without the appearance of Q waves except aVR where one finds RS-T segment elevation and upright T waves. These findings are related to the subendocardial ischemia of coronary insufficiency. On the other hand in acute coronary occlusion with myocardial infarction, Q waves are typical and in leads with significant Q waves the RS-T segment is usually elevated and later T wave inversions appear. In infarction of the posterior wall of the myocardium (diaphragmatic) one may note tall pointed T waves in the right chest V leads.

Bundle branch block, intermittent or permanent, left or right, complete or incomplete, may occur in the presence of coronary artery disease. These patterns may obscure the appearance of significant Q waves with the onset of acute coronary occlusion—especially anterior wall myocardial infarction in a patient with left bundle branch block. However, it should be noted that such block patterns may be functional, positional, respiratory or congenital.

In coronary artery disease, the electrocardiogram may disclose tall, wide P waves, prolongation of the P-R interval, incomplete or complete A-V block, inverted u waves, premature beats and any other arrhythmia. Again, none of the alterations are specific for coronary disease. The Wolff-Parkinson-White pattern may be found in normal individuals as well as those with organic heart disease.

*Diagnostic Value.* The electrocardiogram at rest has been found to be entirely normal in from 25 to 60 per cent of patients with organic coronary artery disease. Therefore, early in the disease one may expect a normal tracing in a large number of individuals and of necessity, one must rely on other cardiac diagnostic tests. Later on in the progress of the disease, the electrocardiogram is more apt to be abnormal and then of diagnostic value in a positive sense. It must be reemphasized that a normal or abnormal electrocardiographic tracing must be interpreted in the light of the entire clinical picture to be of full value. Moreover, when the latter is combined with serial tracings, obscure states may often be resolved correctly and thus prognostic value may be obtained in the resting electrocardiogram.

The absolute necessity for more dependable methods for the diagnosis of coronary artery disease has led to the increasing popularity of the following tests of cardiac function—the “2-step” exercise electrocardiogram<sup>3, 4</sup> and the ballistocardiogram.<sup>5, 8</sup>

#### *“2-Step” Exercise Electrocardiogram*

It has been found that in 25 to 60 per cent of patients with coronary artery disease, the results of all routine investigations may be normal—physical examination, cardiac fluoroscopy, and chest teleroentgenogram. Following the introduction of the “2-step” exercise procedure in 1929, Master later applied the electrocardiographic changes following standard exercise as the test for coronary insufficiency.

*Technique.* After routine examination, the "2-step" test is performed only if the 12 lead resting electrocardiogram is normal. The patient walks over the "2-step" stairs with the electrodes left in place. Each step is nine inches (22.9 cm) high. Routinely standard leads 1, 2, and 3 and precordial lead,  $V_4$  or  $V_5$  (with the tallest, widest R wave) are taken. More recently the four leads recorded are standard lead 2 and precordial leads  $V_3$ ,  $V_4$  and  $V_5$ . In the single test, the required number of ascents (complete trips over the steps in one direction) is determined from a table based upon sex, age and weight. The single test is performed in one-and-one-half minutes and the patient then returns to his original position, sitting or recumbent. The electrocardiogram (4 leads) is recorded immediately, two minutes and six minutes after completion of the exercise. In order to avoid dizziness the direction of the patient is changed after the completion of each trip, that is, he turns toward the examiner each time. In the event that the single test is normal, then a minimum of one hour later the double "2-step" is performed. The latter is twice the number of standard trips in three minutes and is advised only if the single "2-step" is normal, for reasons of safety. The importance of the double exercise is borne out by the fact that one-third of patients with abnormal double tests presented normal single tests.

*Interpretation.* Criteria for abnormal single and/or double "2-step" tests include (1) Depression of the RS-T segment greater than  $\frac{1}{2}$  mm below the isoelectric (P-R) level, (2) Complete or partial inversion of a T-wave (except in lead 3), or (3) transient arrhythmias, conduction defects, or large Q waves. These alterations are identical with the electrocardiographic changes during spontaneous episodes of angina pectoris. The most sensitive leads for this test are the precordial ( $V_4$  or  $V_5$ ). Tracings are repeated beyond six minutes if necessary, until the record returns to the normal control. These electrocardiographic alterations are independent of the appearance of chest pain or pressure and the latter is not a criterion for a positive test. The "2-step" exercise is contraindicated if heart failure, cardiac enlargement or an abnormal resting electrocardiogram is found. Food or exercise within one hour, tobacco, digitalis and nitroglycerin all influence the result of the test.

*Specificity.* Abnormal "2-step" exercise electrocardiograms, single or double, present definite evidence of coronary insufficiency on effort. It must be emphasized that abnormal tests are not specific for coronary artery disease since other organic or functional states may be the underlying cause (rheumatic, luetic or congenital heart disease or severe anemia, for example). On the other hand the "2-step" test may be abnormal in from 6 to 8 per cent of normal people and also in patients with neurocirculatory asthenia or anxiety states. Differentiation between such functional states and true organic heart involvement may be made usually on clinical grounds alone. However, we have found dihydroergocornine (DHO-180), a "sympatholytic" agent, of value in this regard.

*Diagnostic Value.* The value of the "2-step" exercise test has been corroborated by a five year follow-up study of hundreds of patients. If both

the single and double "2-step" tests are normal, a diagnosis of coronary insufficiency and hence, coronary artery disease, is practically (but not absolutely) excluded. Thus, the value of the "2-step" test in the negative sense is inestimable. On the other hand, in patients with normal resting electrocardiograms, an abnormal single or double "2-step" test presents objective evidence of coronary insufficiency. The decision of a final label of coronary artery disease rests with the examining physician after correlation of the abnormal results of the exercise with the clinical status of the patient.

### *Ballistocardiography*

In 1949 with the introduction of the direct body recording technique by Dock and Taubman,<sup>6</sup> the ballistocardiograph became available generally as a practical cardiac function test. The ballistocardiogram is a record of the motion of the body induced by the contraction of the heart and the surge of blood into the arterial tree during each cardiac cycle. We have investigated the ballistocardiograph in over 2,000 patients during the past four years and have utilized a modified Dock type instrument, the Pordy dual ballistocardiograph for recording both photoelectric (displacement) and electromagnetic (velocity) tracings with a single setting. A report of the accuracy of this apparatus as checked mechanically with linear reciprocating motion by Dr. Sergei Feitelberg is in progress.

*Technique* The patient lies supine on a fixed, immobile table. A cross-bar placed on the shins transmits the longitudinal body motions (without a hinge) by cutting light falling on the photo-cell and/or by altering an electromagnetic field. The record is taken on the customary electrocardiographic machine by direct attachment to the lead 1 electrodes. Whenever time reference is desired, simultaneous electrocardiograms and ballistocardiograms may be recorded simply, even on the routine single channel electrocardiographs. The ballistocardiogram is recorded during quiet respiration and then deep inspiration and finally deep expiration.

*Interpretation* Ballistocardiograms, like electrocardiograms, may be read by direct inspection of the record. The normal ballistocardiogram is of a W-shaped appearance, with the base-line one which bisects the waves. By convention, headward motion of the body is represented as an upward deflection on the record and *vice versa*. The component waves are labeled in alphabetical order according to Starr, commencing with the letter "H". This represents the first headward motion with each cardiac cycle and is related to the apical thrust. The I-wave represents the recoil of the body to ejection in early systole. The most prominent headward wave is the J-wave and this results from impact on the aortic arch and acceleration of blood in the aorta. The K-wave is the most prominent footward deflection and is related to deceleration in the descending aorta. L, M, N and O, and so on, are the diastolic after vibrations or actually forced thrusts.

The records are interpreted on the qualitative appearance of the component waves of the ballistocardiogram and we have not attempted their use quantitatively as a measure of cardiac output. In normal persons,

there is a respiratory variation in the amplitude of the complexes, being of greater amplitude in inspiration than in expiration. Criteria for abnormality include: (1) diminished or absent I-waves, (2) exaggeration of the normal respiratory variation so that the amplitude of the waves during expiration is 50 per cent or less than during inspiration, (3) slurring or notching of I, J, or K-waves, (4) early "M" pattern—prominent H-waves, (5) late "M" pattern—late, deeply notched J-waves, (6) prominent diastolic waves (L, M, N, O, and so on), (7) deep, wide or absent K-waves, or (8) low amplitude or totally bizarre complexes. Any one record may display one alteration alone or various combinations. Moreover, abnormal waves may be detected in only one phase of respiration. For example, in early coronary disease alterations may appear in the complexes only during the expiratory phase.

*Specificity* Like the resting and "2-step" exercise electrocardiogram, there is no ballistocardiographic pattern specific for coronary artery disease. The factor of age plays an important role in interpretation. Under the age of 50 one would expect to find a normal ballistocardiogram almost routinely. Therefore, an *abnormal* tracing in a coronary disease suspect under 50 is of great significance diagnostically, since thereafter the record may be altered by physiological aging processes. On the other hand a *normal* ballistocardiogram in a patient over 50 would correlate well with a normal cardiovascular tree. It must be pointed out that in patients with coronary artery disease who undergo complete functional recovery, the ballistocardiogram and the resting as well as exercise electrocardiogram may return to normal.

*Diagnostic Value* Ballistocardiography has its greatest application in the diagnosis of coronary artery disease. In patients with angina pectoris and abnormal resting electrocardiograms, 93 per cent presented abnormal ballistocardiograms as well. Moreover, in 85 per cent of patients with angina pectoris, normal resting electrocardiograms but abnormal "2-step" exercise tests, the ballistocardiograms *at rest* were abnormal. The use of standard exercise ballistocardiograms increased this figure to 90 per cent. In early cases of coronary artery disease, cardiac ejection may be altered only following exertion. Therefore, the ballistocardiogram should be recorded after standard exercise if the resting record is normal. A close correlation was found between abnormal "2-step" exercise tests and abnormal resting ballistocardiograms. Both should be employed routinely in the detection of coronary artery disease since one records electrical and the other mechanical events.

The high percentage of abnormal ballistocardiograms in hypertensive patients limits its value somewhat in the diagnosis of coronary artery disease. In patients with acute myocardial infarction, the ballistocardiogram becomes abnormal and may return to normal (in 19 per cent) usually paralleling functional recovery. Thus the value extends to prognosis in coronary disease patients. In the diagnosis of coronary disease, the ballistocardiogram offers a simple means of early detection with the advantage of lack of any danger to the patient. The use of the tobacco

ballistocardiographic test may enhance the diagnostic value of this procedure in coronary disease

### *Conclusion*

The clinical status and routine examination of the patient should be correlated with the results of a battery of tests—the electrocardiogram, the Master “2-step” exercise test and the ballistocardiogram—for the final, early and accurate diagnosis of coronary artery disease

### SUMMARY

- 1 The scope of the problem of the diagnosis of coronary artery disease is discussed
- 2 The value and limitations of routine electrocardiography is outlined
- 3 The Master “2-step” exercise test is described and the diagnostic value is stressed
- 4 The ballistocardiogram is presented as a valuable means for early detection of coronary disease

### RESUMEN

- 1 Se discute el alcance del problema del diagnóstico de la afección de la arteria coronaria
- 2 Se presenta el valor y las limitaciones de electrocardiografía de rutina
- 3 El ejercicio “Master two step” se detalla y se subraya su valor diagnóstico
- 4 Se presenta el balistocardiograma como un valioso medio para el descubrimiento temprano de la afección coronaria

El estado clínico y el examen de rutina del enfermo deben ser correlativos con el resultado de las pruebas en batería o grupe el electrocardiograma, el ejercicio “Master two step” y el balistocardiograma, a fin de hacer un diagnóstico final y exacto de la enfermedad coronaria

### RESUME

- 1) L'auteur met en discussion la question du diagnostic de l'atteinte de l'artère coronaire
- 2) Il insiste sur la valeur et sur les limites de l'électrocardiogramme habituel
- 3) Il précise la valeur du test essentiel de l'exercice dit “des deux pas” et son importance au point de vue du diagnostic
- 4) Il considère le ballistocardiogramme comme un moyen valable pour découvrir précocément l'atteinte coronarienne

L'état clinique et l'examen systématique du malade doivent être conjugués à ce que donne toute une série de tests électrocardiogramme, exercice “des deux pas,” ballistocardiogramme. Ainsi le diagnostic des maladies coronariennes pourra être définitif, précoce et précis



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# The Vectorcardiographic Diagnosis of Myocardial Infarction

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Interest in spatial vectorcardiography has grown considerably in the past 15 to 20 years, and increasing numbers of workers are investigating the method and probing its diagnostic usefulness. There is still a great deal of disagreement concerning fundamental issues, largely the result of lack of unanimity in regard to methods, and views concerning its value compared to the electrocardiogram are at considerable variance.

Preliminary experience in this laboratory led to the unqualified opinion that spatial vectorcardiography contributes to the basic understanding of the electric phenomena associated with the heart beat, and reveals diagnostic clues unknown or impossible in electrocardiography.<sup>1</sup> The conclusion was reached that right and left ventricular hypertrophy, singly or combined, intraventricular block, and myocardial infarction are disclosed more often and more clearly by the vectorcardiogram than by the electrocardiogram. Our continued experience in this field has strengthened this point of view. Since there are no generally accepted diagnostic criteria in vectorcardiography, this opinion is based, for the most part, on a comparison of vectorcardiographic and electrocardiographic interpretation. Consequently, the electrocardiographic interpretation, being at present the more generally acceptable, serves as the standard. A more satisfactory approach to the problem was attempted in relation to posterior myocardial infarction, and appeared to substantiate the earlier impressions.<sup>2</sup>

A larger study has now been completed, constituting our total experience to date. This embraces a comparison of vectorcardiographic and electrocardiographic interpretation with pathologic correlation in 50 consecutive cases which came to autopsy.<sup>3</sup> The data strikingly demonstrate the superiority of the vectorcardiogram. Among the 50 cases were 22 (exclusive of those with left bundle branch block) in which autopsy showed myocardial infarction, and 10 of these, selected at random, are presented below. The pertinent clinical and pathological data, and the electrocardiographic and vectorcardiographic diagnoses are listed in Table I.

## *The Vectorcardiographic Diagnosis of Myocardial Infarction*

At each instant during cardiac systole all electric forces summate into one manifest force having magnitude, direction, and sense. This manifest force is called the cardiac vector and the projection of its terminus on various planes from instant to instant throughout systole traces the vectorcardiographic loop. Electrocardiographic leads, on the other hand,

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TABLE I

Case No	Sex Age	Clinical Diagnosis	Vectorcardiographic Interpretation	Electrocardiographic Interpretation	Pathologic Data
1	M 62	Coronary Heart Disease Acute M I Pulmonary emphysema Pulmonary Edema	10/22/51 Inferior, anterior, and septal M I R and L V H L O U* R A D†	10/23/51 Acute postero-lateral M I	10/26/51 Fresh post, and septal M I Anterior wall not sampled L and R V H (4, 5, 6)**
2	M 58	A S H D C H F Diabetes Hemochromatosis Uremia	7/23/52 High post and ant-lateral M I Acute Pericarditis L and R V H R A D L P D	7/22/52 Arborization block Acute antero-lateral M I Acute pericarditis	7/24/52 Old ant., post, lateral M I Fresh ischemic necrosis apex Diffuse fibrinous pericarditis L and R V H (1, 2, 3, 4, 5, 7, 8)
3	M 52	A S H D C H F Old M I Low salt syndrome	10/4/51 Inferior, anterior, lateral M I L and R V H R A U L A D	10/4/51 Healed postero-lateral M I	11/6/51 Posterior, anterolateral, and septal M I L and R V H (2, 3, 5, 6)
4	F 72	Coronary H D Acute M I Pulmonary infarct A F C H F Pulmonary emphysema	10/11/51 Inf, ant M I R and L V H R A U L P D	10/11/51 Acute ant and acute post M I	11/7/51 Healing postero-septal and ant M I L and R V H (7, 8, 9)
5	M 77	A S H D A P A F Old M I ? Acute M I C H F Pulmonary emphysema	12/11/51 Anterior and Septal M I L V H L P D R P U	12/11/51 Anterior and septal M I I V Block	3/9/52 Old anterior and septal M I Also posterior M I Possible L and R V H (4, 5, 6, 7, 8, 9)
6	M 67	Hyp and Cor H D Old M I C F Asthma Chronic Bronchitis Emphysema ? Pulm Infarct	1/22/52 Ant, Inf, Septal M I R. and L V H L P U L P D	1/25/52 Antero-septal M I L V H	5/15/53 Anteroseptal, posterior, apical, lateral fibrosis L and R V H (5, 7, 8)
7	M 62	A S H D Old and Acute M I C H F Diabetes	12/17/51 Anterior, inferior, postero-lateral M I I V Block R A U L P D	12/17/51 Infero-lateral M I L V H	3/7/52 Antero-lateral and posterior fibrosis R and L V H possible (2, 3, 4, 5, 6, 7)
8	F 57	Old M I C H F Avitaminosis	1/6/54 Anterior, high postero-septal M I L V H L A D R A D	1/8/54 Anterior M I	1/15/54 Anterior, posterior, and septal M I R V M I L and R V H (2)

are scalar derivatives of the cardiac vector, and are characterized by magnitude and sense only. The vectorcardiogram, therefore, permits an analysis of initial and early depolarization forces which is superior to the electrocardiogram. Except in situations in which the left ventricle is activated belatedly, as in left bundle branch block, or in an aberrant manner, as in anomalous atrioventricular excitation, these initial and early forces hold the clue to the diagnosis of infarction<sup>1, 4, 5</sup>

Previous observations have shown that the initial and early depolarization forces have a characteristic orientation in various heart positions in the absence of localized myocardial disease<sup>6</sup>. The effect of the extrinsic

TABLE I

Case No	Sex Age	Clinical Diagnosis	Vectorcardiographic Interpretation	Electrocardiographic Interpretation	Pathologic Data
9	M 67	Coronary H D Angina Acute M I Aortic stenosis Pulmonary emphysema C H F Diabetes	10/8/51 Posterior and septal M I R and L V H R B B B R P U R A D	10/16/51 Posterior, and acute extensive anterior M I L V H R B B B	10/20/51 Anterior, posterior, and septal fibrosis L and R V H (Insufficient sampling of ant wall) (1, 5, 6)
10	M 60	A S H D Old M I Acute M I Emphysema Old pulmonary infarct. C H F	12/12/52 Anterior, posterior, septal M I L V H L P U R P U	12/12/52 L B B B	2/24/53 Old posterior M I L V H ? R V H (4, 5, 6)

Age, sex, clinical diagnosis, vectorcardiographic and electrocardiographic interpretation, and pathologic findings. Date of taking the vectorcardiogram and electrocardiogram, and on which the autopsy was done, is given in the upper left hand corner of the appropriate box.

M = Male F = Female

M I = Myocardial infarction

A S H D = Arteriosclerotic heart disease

C H F = Congestive heart failure

H D = Heart disease

A F = Auricular fibrillation

A P = Angina pectoris

R and L V H = Right and left ventricular hypertrophy

Post. = Posterior

Ant. = Anterior

Inf = Inferior

I V Block = Intraventricular block

Hyp and Cor H D = Hypertensive and coronary heart disease

Pulm Infarct = Pulmonary infarct

R B B B = Right bundle branch block

L B B B = Left bundle branch block

\*Direction of initial forces } L = Left R = Right  
A = Anterior P = Posterior  
†Direction of terminal forces } D = Down U = Up

\*\*Areas involved on posterior wall of left ventricle (2)

The numerals in the bottom line of each box in the column of Pathologic Data refer to involved areas (2)

factors, position and rotation, can be recognized, therefore, and distinguished from intrinsic factors, in the normal heart, in right and left ventricular hypertrophy, and in right and left bundle branch block. These forces represent the summation, from instant to instant, of the forces of depolarization of all the individual muscle fibers activated at the onset and early in ventricular systole. During this interval there are fewer fibers being activated than later when the entire ventricular mass is in the active state. The early part of the QRSsE loop, therefore, is less complex than the subsequent portions. When infarction occurs, or when myocardial fibers become irresponsive as the result of sub-lethal injury, the involved fibers are rendered electrically inert, and there is a new balance of forces. The new resultants are modified both as regards their spatial position and their magnitude, they tend to point away from the electrically inert areas. Although these changes may take place throughout the entire period of ventricular depolarization, modification of the early, less complex part of the curve is probably greater, and more easily recognized, than the alterations occurring later. The diagnostic changes, consequently, are more evident in the initial and early forces, than in the overall disposition of the loop.

It is necessary to have clearly in mind the spatial position of the initial and early forces of the normal vectorcardiogram, and alterations in these which are dependent exclusively on changes in position and rotation. The disposition of the terminal forces is sometimes of great help in determining heart position. Myocardial infarction is suspected if the orientation of the early forces cannot be accounted for entirely on the basis of extrinsic factors. Infarction of the interventricular septum is indicated by abnormal initial forces, and of the free wall of the left ventricle by abnormal early forces. Abnormal direction of inscription of the QRS loop is also diagnostic of free wall infarction.

If the QRSsE loop does not begin and end at the same point (O point), the loop is said to be open, and corresponds to S-T segment deviation in the electrocardiogram. In open loops the spatial relationship between the O point and the end of the loop is characteristic in acute anterior and posterior infarction, ventricular hypertrophy, and acute pericarditis. The T loops have an altered direction of inscription in infarction, and are long and narrow in acute, and small and round in healing and old infarction.

#### *Description and Interpretation of Vectorcardiograms in Myocardial Infarction*

*Figure 1* The initial QRS forces are oriented to the left and up, and therefore, are abnormal, indicating disease of the interventricular septum. The early forces continue in an exaggerated posterior and upward direction, and are diagnostic of infarction of the anterior, and lower part of the posterior wall of the left ventricle. The QRS loop ends to the right, anteriorly, and inferiorly to the O point, resulting in an open QRSsE loop of the type seen in acute anterior and posterior infarction.

The clockwise inscription of the frontal, and counterclockwise inscription of the sagittal projections, is abnormal. This is frequently observed in posterior wall infarction, but also occurs in combined right and left ventricular hypertrophy.

Histologic correlation is excellent, and superior to that of the electrocardiogram (See Table I).

*Figure 2* The initial QRS forces point to the right, anteriorly, and down, which is normal for a horizontally placed loop. However, the continued rightward, anterior, and downward orientation of the early forces is characteristic of a high postero-lateral lesion. Nevertheless, quite early

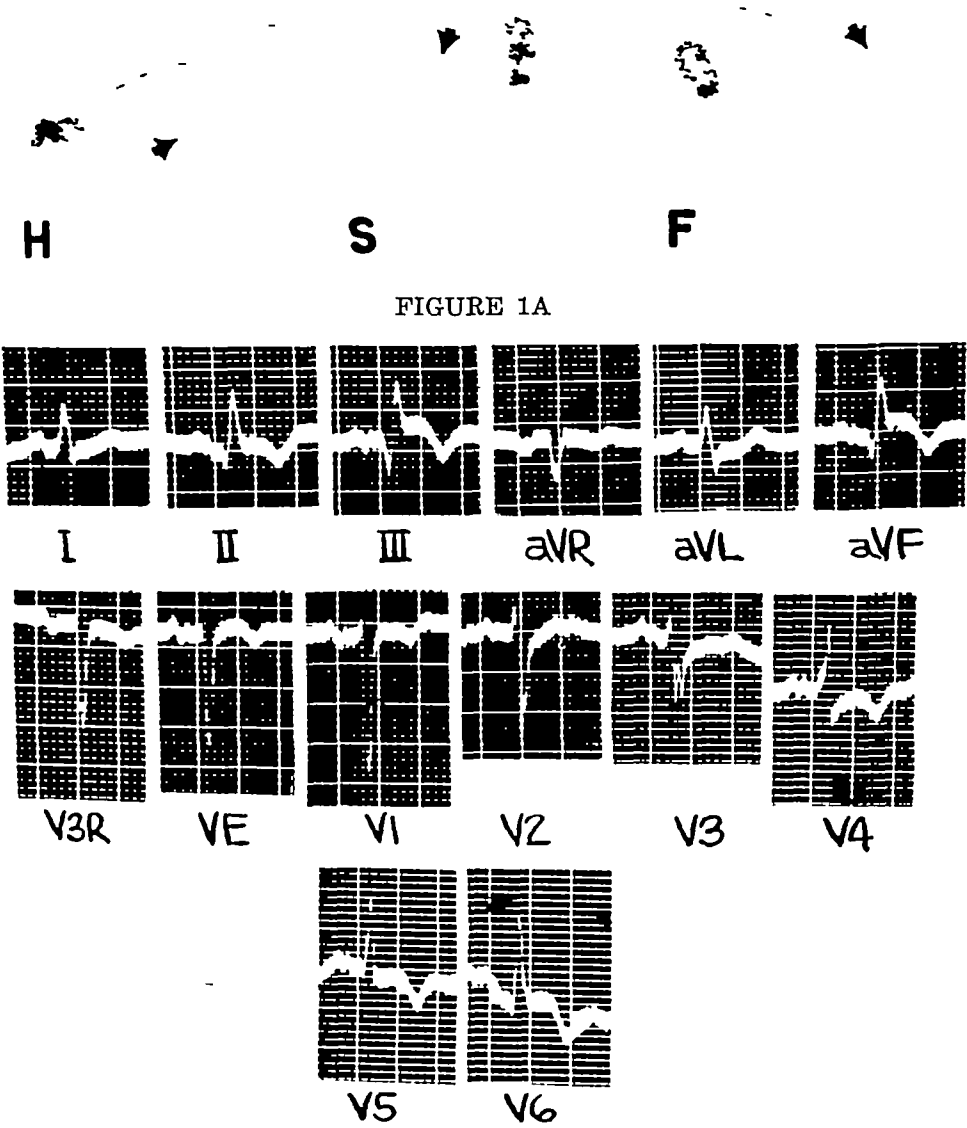


FIGURE 1B

*Figure 1A* Vectorcardiogram in fresh posterior and septal myocardial infarction. Anterior wall not sampled. Left and right ventricular hypertrophy. In this and the following figures H = Horizontal, S = Sagittal, and F = Frontal plane projections, and arrows indicate direction of inscription of the QRS loop. See text and Table I.—  
*Figure 1B* Electrocardiogram from same patient.

in the QRS interval there is pronounced posterior displacement, resulting in clockwise inscription of the horizontal projection, striking abnormalities which indicate anterior wall infarction

The end of the QRS loop is to the left of, and anterior and inferior to the point of origin, a relationship which is characteristic of acute fibrinous pericarditis

The clockwise inscription of the horizontally placed frontal loop, which

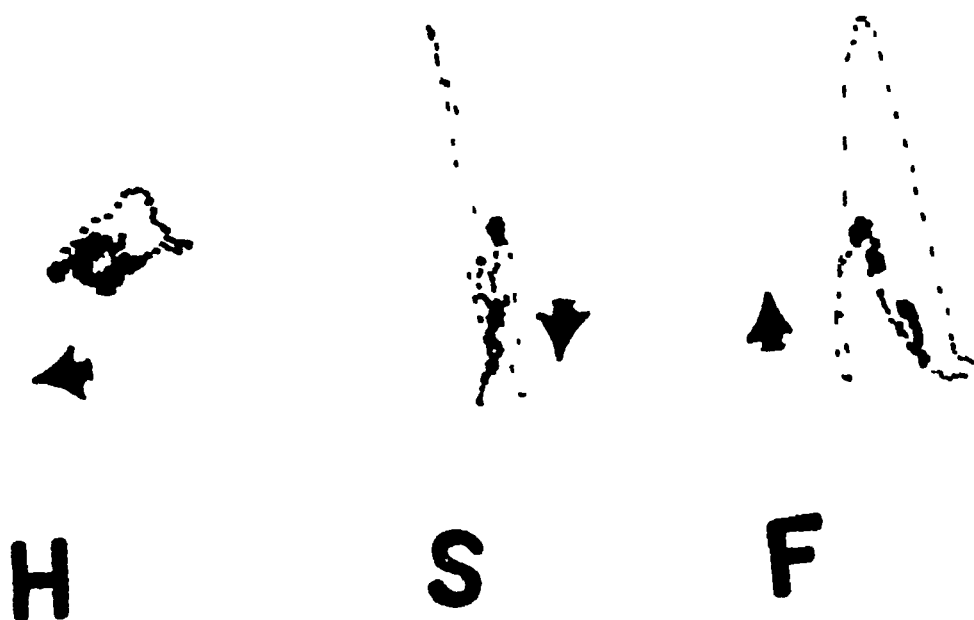


FIGURE 2A

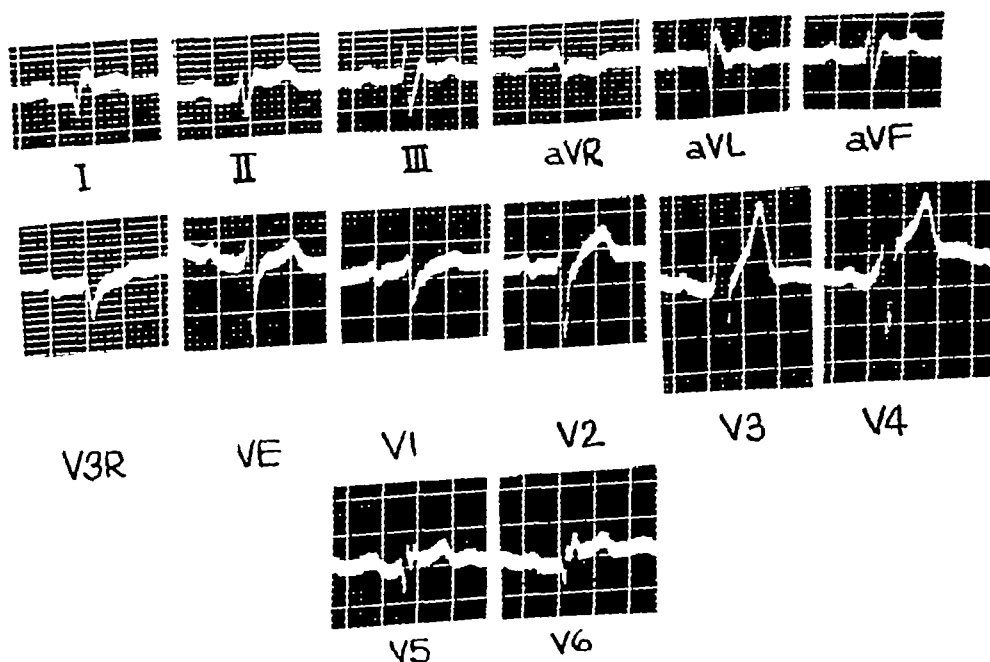


FIGURE 2B

Figure 2A Vectorcardiogram in old anterior, posterior, and lateral wall infarction and diffuse fibrinous pericarditis (uremic) Fresh apical ischemic necrosis Left and Right Ventricular Hypertrophy See text and Table I—Figure 2B Electrocardiogram from same patient

has features seen in left ventricular hypertrophy, is due to the infarct, or to right ventricular hypertrophy

Histologic correlation is excellent, and greatly superior to that of the electrocardiogram

*Figure 3* There is no evidence of septal involvement, since the initial forces have a rightward, anterior, and barely upward orientation, which is normal in a horizontal loop. The early forces, however, continue far to the right, then swing sharply to the left, posteriorly, and upwards, denoting anterior, inferior, and lateral wall myocardial infarction. The QRS loop is closed and the T loops are rather small, indicating healed infarction.

The direction of inscription in each projection is the reverse of that expected in the normal, a common finding in infarction. However, clockwise inscription of a markedly horizontal frontal loop suggests right and left ventricular hypertrophy.

Histological correlation with the vectorcardiographic interpretation is good, and far superior to the electrocardiographic interpretation.

*Figure 4* Septal involvement is excluded because the initial forces are normal (right, anterior, and barely superior). The early forces turn



FIGURE 3A

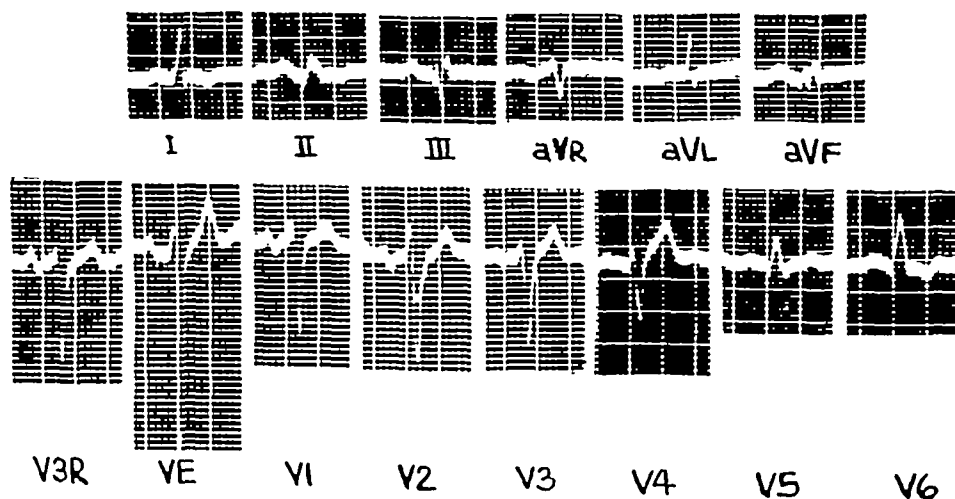


FIGURE 3B

*Figure 3A* Vectorcardiogram in posterior, antero-lateral, and septal myocardial infarction. Left and Right Ventricular hypertrophy. See text and Table I—*Figure 3B* Electrocardiogram from same patient.



sharply posteriorly, superiorly, and to the left. From then on the loop remains posterior, superior, and to the left. These features are diagnostic of inferior and anterior myocardial infarction. The counterclockwise and clockwise inscription of the sagittal and frontal loops, respectively, occurs in infarction. However, clockwise inscription of a markedly horizontal frontal loop suggests right and left ventricular hypertrophy.

The QRS loops are only slightly open, and the T loops are small, the infarction is healing or old.

Correlation of the pathologic findings with the vectorcardiographic diagnosis is good. Only the septal involvement was missed. The electrocardiographic interpretation did not correlate as well, the infarction was thought to be acute, and the hypertrophy was not recognized.

*Figure 5* The abnormal initial forces (left, posterior, and down), and the posterior displacement of the early forces, signify lesions in the interventricular septum, and in the anterior wall of the left ventricle, respectively.

The markedly horizontal position of the loop is strongly suggestive of left ventricular hypertrophy.

*Correlation* The vectorcardiogram anticipated everything found at

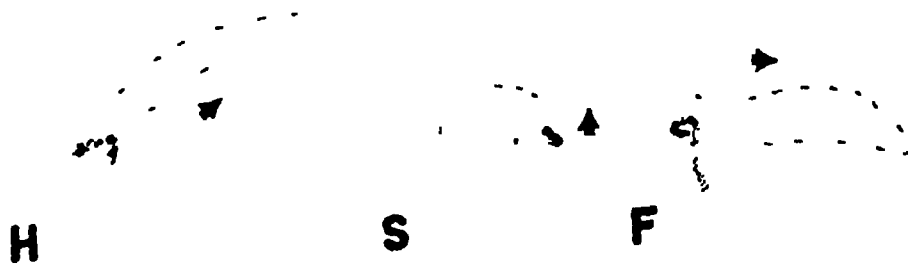


FIGURE 4A

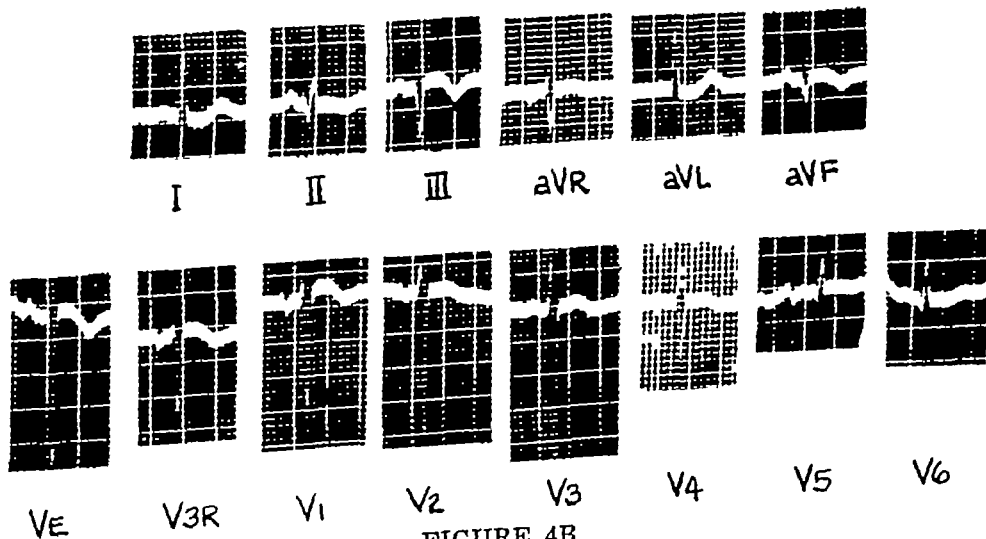


FIGURE 4B

*Figure 4A* Vectorcardiogram in healing postero-septal and anterior myocardial infarction. Left and Right Ventricular Hypertrophy. See text and Table I—*Figure 4B* Electrocardiogram from same patient.

autopsy except the laige posterior infarct The posterior infarct and the left ventricular hypertrophy as well, were missed in the electrocardiogram

*Figure 6* The vectorcardiogram was interpreted as showing infarction of the anterior, inferior (diaphragmatic), and septal walls, and right and left ventricular hypertrophy The initial forces (left, posterior, and up) call attention to the septal lesion, and the displacement of the early forces posteriorly and superiorly indicate anterior and inferior wall disease, respectively The reversal in direction of inscription of all projections is common in infarction, but the clockwise inscription of the horizontally placed frontal loop suggests left and right ventricular hypertrophy



FIGURE 5A

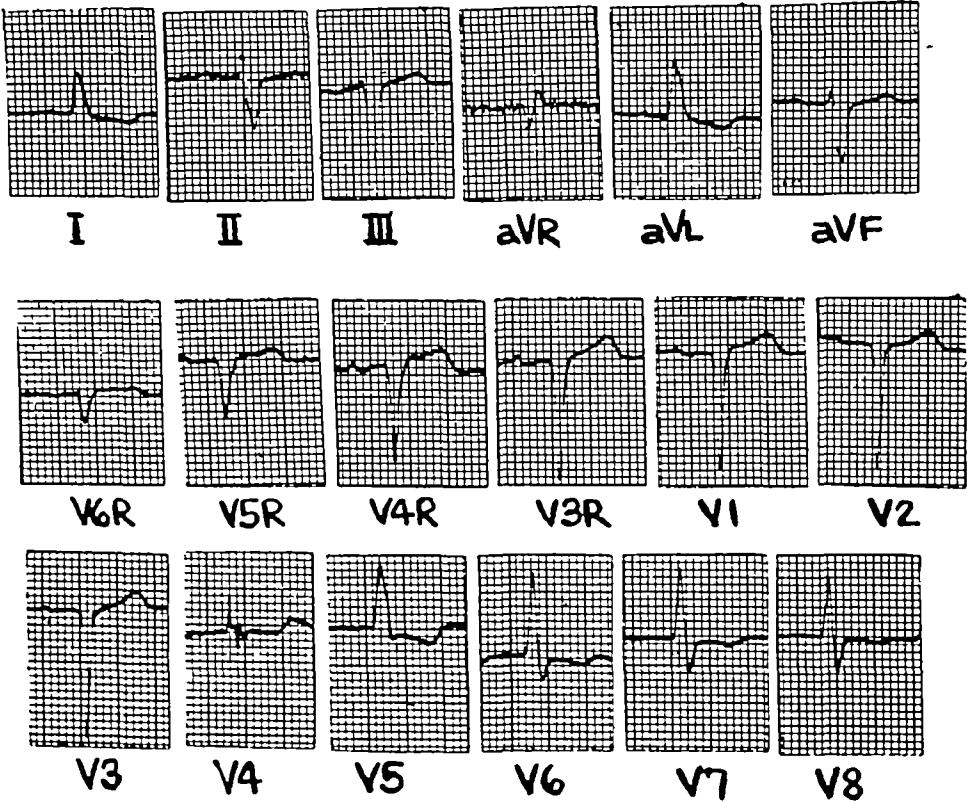


FIGURE 5B

*Figure 5A* Vectorcardiogram in old anterior, posterior, and septal myocardial infarction Possible left and right ventricular hypertrophy See text and Table I—  
*Figure 5B* Electrocardiogram from same patient

Correlation of the vectorcardiographic diagnosis with the autopsy findings is excellent, and greatly superior to the electrocardiogram

*Figure 7* Clockwise inscription of the posteriorly placed horizontal projection is characteristic of anterior wall infarction, and upward displacement of the early forces in a horizontally placed frontal loop is characteristic of an inferior lesion. Marked rightward displacement of the early forces seen in the horizontal and frontal projections indicates involvement of the lateral wall. The initial forces are normal (right, anterior, and barely up) and a diagnosis of septal infarction was not made. The markedly horizontal position of the loop suggests left ventricular hypertrophy.

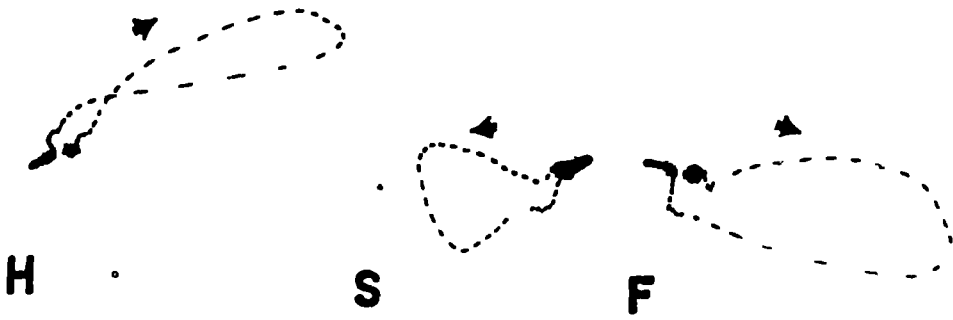


FIGURE 6A

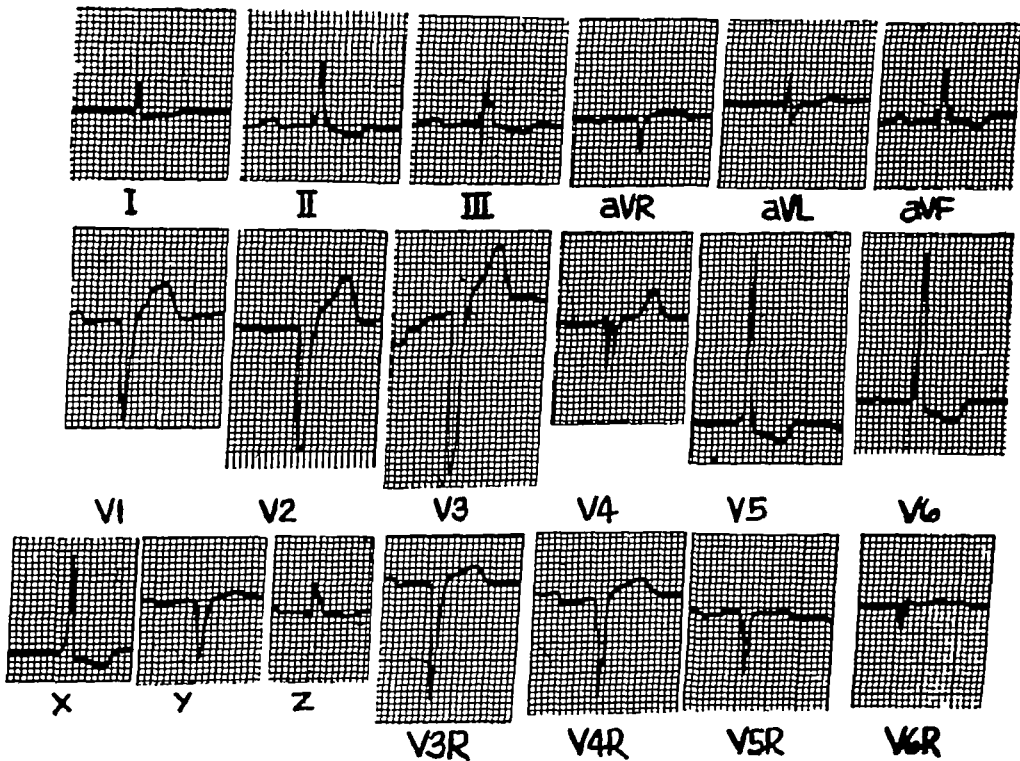


FIGURE 6B

*Figure 6A* Vectorcardiogram in anteroseptal, posterior, apical and lateral wall fibrosis Left and Right Ventricular Hypertrophy. See text and Table I—*Figure 6B* Electrocardiogram from same patient

Correlation with the autopsy findings is excellent and superior to that of the electrocardiogram

*Figure 8* The vectorcardiogram was interpreted as showing an extensive myocardial infarct involving the postero-basal and septal myocardium, and the anterior wall. The abnormal initial forces (left, anterior, down) indicate a septal lesion, and continuation of the early forces in the same direction is diagnostic of postero-basal infarction. The almost completely posterior orientation of the spatial loop was considered evidence of extensive anterior myocardial infarction. The horizontally placed frontal projection suggests left ventricular hypertrophy.

Correlation with the autopsy findings is good, and greatly superior to the electrocardiogram

*Figure 9* The most obvious abnormality is clockwise inscription of the anteriorly placed horizontal projection, which is diagnostic of right ventricular hypertrophy, and the clockwise inscription of the horizontally placed frontal loop, which is characteristic of right and left ventricular hypertrophy. The terminal forces indicate right bundle branch block.

The abnormal initial forces (right, posterior, and up), and the abnormal upward displacement of the early forces, indicate septal and inferior myocardial infarction, respectively. The bizarre sagittal loop is due partly to rotation.



FIGURE 7A

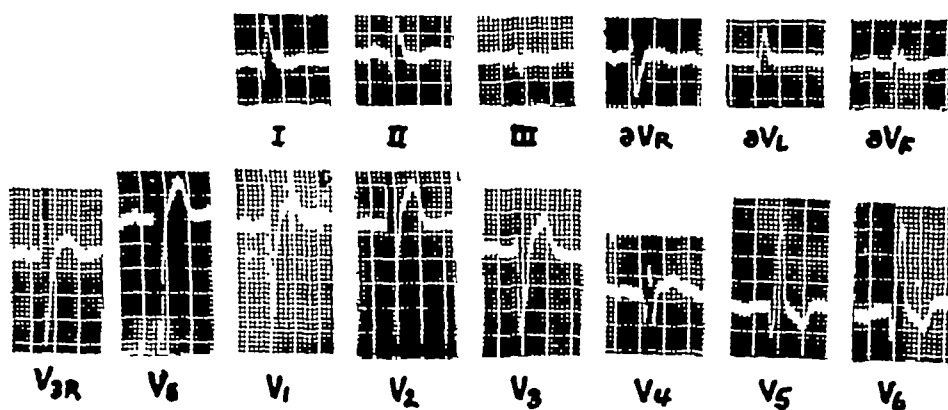


FIGURE 7B

*Figure 7A* Vectorcardiogram in antero-lateral and posterior wall fibrosis. Right and Left Ventricular Hypertrophy possible. See text and Table I—*Figure 7B* Electrocardiogram from same patient.

Correlation with the autopsy findings is fair, and not as good as that of the electrocardiogram

*Figure 10* The abnormal initial and early forces (left, posterior, and up) indicate septal, inferior, and anterior wall infarction. The terminal forces are characteristic of left ventricular hypertrophy.

Correlation with the autopsy findings is excellent, and far superior to that of the electrocardiogram.

### Discussion

The above observations clearly indicate that the vectorcardiogram is capable of revealing the presence of myocardial infarction. The cardiac vector is analyzed in relation to the three natural coordinate axes of the body as revealed by projection onto three mutually perpendicular planes, horizontal, sagittal, and frontal.<sup>1</sup> Except in instances of unusual heart position, displacement of electrical forces in the antero-posterior axis occurs in anterior and high posterior wall lesions, in the transverse axis in lateral wall and septal region, and in the vertical axis in lesions involving the inferior or basal portion of the posterior wall of the left ventricle. The abnormal vectors are oriented posteriorly and down in anterior infarction, anteriorly and down in high posterior infarction, up

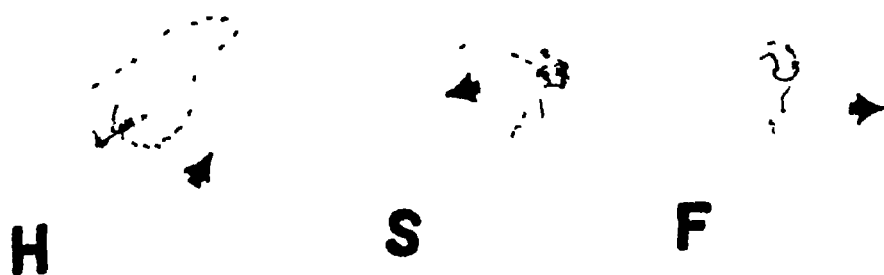


FIGURE 8A

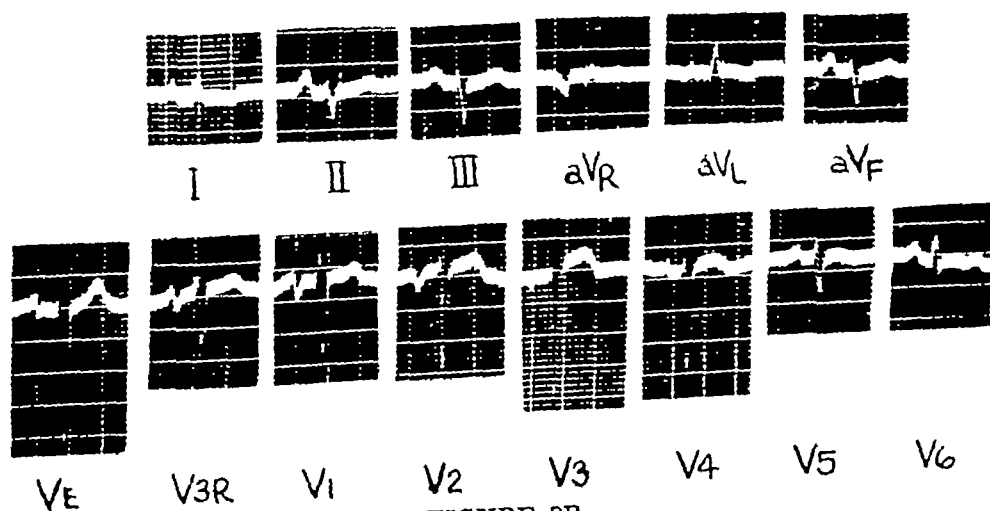


FIGURE 8B

*Figure 8A* Vectorcardiogram in anterior, posterior, and septal myocardial infarction. Also infarction of right ventricular wall. Right and Left Ventricular Hypertrophy. See text and Table I—*Figure 8B* Electrocardiogram from same patient.

and posteriorly in infero-posterior wall lesions, to the left in lesions close to the interventricular septum, and to the right in lateral wall involvement

Any departure from the normal orientation of the initial forces which cannot be explained by extrinsic factors, ventricular hypertrophy, or intraventricular block, indicates a septal lesion

Acute infarction is characterized by an open QRS loop and long narrow T loops. In healing or old infarction the QRS loop tends to close and the T loop is small and round.<sup>7</sup> The manner in which the QRS loop is open is very helpful in differential interpretation. The end of the loop, in relation to the O point, is to the right, anterior, and up in acute anterior myocardial infarction, right, posterior, and down in posterior myocardial infarction, left, anterior, and down in acute fibinous pericarditis, right and up, with no or minimal antero-posterior deviation in left ventricular

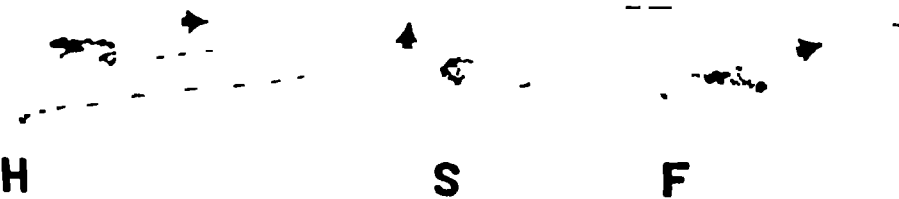


FIGURE 9A

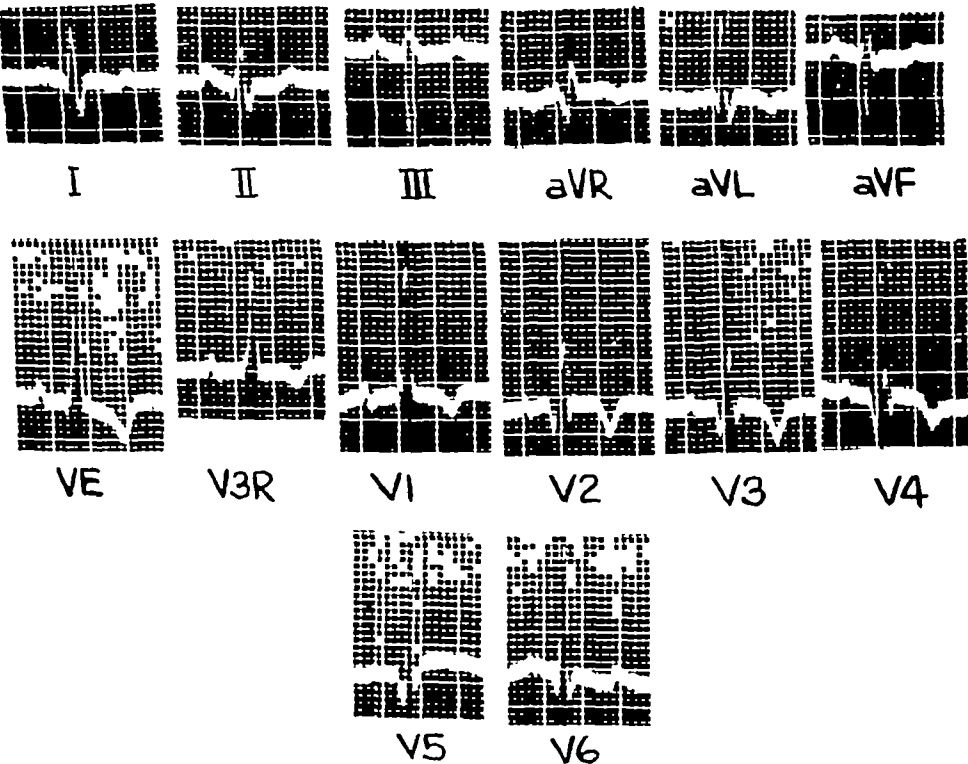


FIGURE 9B

Figure 9A Vectorcardiogram in anterior, posterior, and septal fibrosis. Left and Right Ventricular Hypertrophy. See text and Table I—Figure 9B Electrocardiogram from same patient.

hypertrophy, and left, posterior, and up in right ventricular hypertrophy.

These criteria for the diagnosis of myocardial infarction apply to the reference system used in this laboratory<sup>1</sup>

A comparison of the vectorcardiographic and electrocardiographic interpretations shown in Table I indicates superiority of the vectorcardiogram. The ten cases were chosen at random from a group of 50 cases studied histologically. Analysis of the entire autopsy series reveals an unqualified superiority of the vectorcardiogram over the electrocardiogram in disclosing myocardial infarction, as well as right and left ventricular hypertrophy, singly and in combination.<sup>3</sup> The results are summarized in Table II.

TABLE II  
Vectorcardiographic and electrocardiographic diagnosis, and location at autopsy, of infarcted areas in 22 cases of myocardial infarction. Cases with Left Bundle Branch Block excluded

Location of Infarct	No Cases at Autopsy*	No Diagnosed by Vectorcardiogram	Per Cent	No Diagnosed by Electrocardiogram	Per Cent
Anterior	14	11	79	8	57
Posterior	21	16	76	12	57
Anterior and Posterior	13	10**	75	4**	30
Septum	17	11	65	6	35
Lateral	12	4	33	3	25
Anterior, Posterior, Lateral, and Septum	8	6†	75	2†	25
Any Location	22	18††	82	17††	77

\*Cases with left bundle branch block excluded

\*\*Diagnosis of anterior and posterior myocardial infarction

†Three or more areas diagnosed

††Diagnosis of infarction, irrespective of its localization

The bottom line in Table II is misleading, since it appears to indicate that there is no difference between the two methods of examination. However, the method of selection of patients is responsible for this, as in one experimental group only those cases were chosen for vectorcardiographic study whose electrocardiograms displayed the characteristic signs of infarct.\* The overall results for the diagnosis of myocardial infarction are, therefore, heavily weighted in favor of the electrocardiogram. In spite of this, the data relating to localization and extent of infarction are obviously in favor of the vectorcardiogram. Furthermore, our total clinical experience, which does not have the authority of postmortem confirmation, has demonstrated the superiority of the vectorcardiogram in the diagnosis of infarction.

\*Other groups included patients with hypertension, chronic pulmonary disease, rheumatic heart disease, congenital heart disease, and so on.

High posterior, and some anterior lesions are easily recognizable in the vectorcardiogram, but not in the electrocardiogram. Multiple infarcts appear to make the electrocardiogram more vulnerable, but do not impair the diagnostic usefulness of the vectorcardiogram. The vectorcardio-

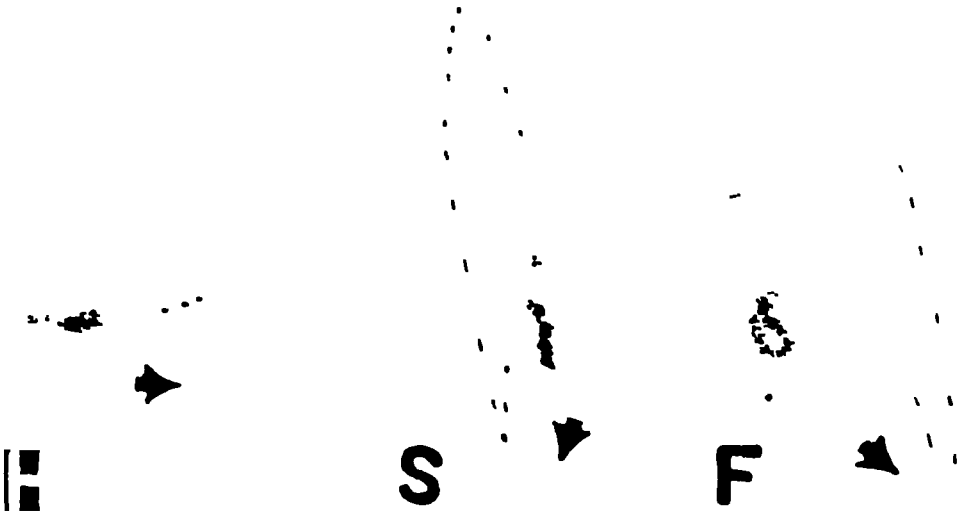


FIGURE 10A

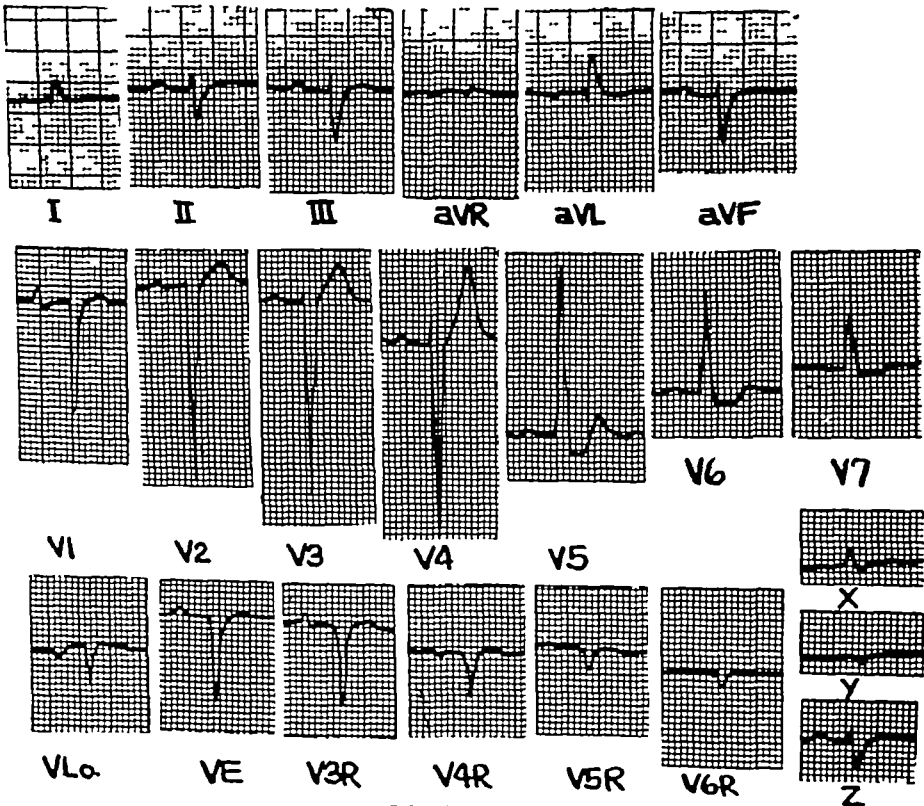


FIGURE 10B

Figure 10A Vectorcardiogram in old posterior myocardial infarction. Left ventricular hypertrophy. Right ventricular hypertrophy. See text and Table I—Figure 10B. Electrocardiogram from same patient.



gram does much better than the electrocardiogram in disclosing septal lesions, while both are poor indicators of lateral wall infarcts. A diagnosis of isolated septal infarction was made in only one case, by vectorcardiogram, but as in previous studies, the autopsy data indicate that free wall infarction always accompanies septal infarction<sup>2, 8</sup>. Similarly, isolated lateral wall infarction does not occur.

Right and left ventricular hypertrophy, singly and combined, can be recognized much more readily in the vectorcardiogram than in the electrocardiogram. This is even more strikingly apparent when hypertrophy and infarction coexist.

A false diagnosis of myocardial infarction is one of the serious pitfalls in the laboratory diagnosis of coronary heart disease. In the series referred to, however, a vectorcardiographic diagnosis of myocardial infarction was not made in a single instance in which autopsy failed to disclose such a lesion. On the other hand, one such electrocardiographic error was made. While not a single false vectorcardiographic diagnosis of myocardial infarction was made, over diagnosis occurred three times. In these three cases the diagnosis of anterior wall infarction was not confirmed at autopsy, although infarction existed elsewhere. A similar error in electrocardiographic diagnosis was made, also in three cases. In two additional cases a diagnosis of anterior infarction was made by vectorcardiogram and electrocardiogram but pathologic correlation was impossible as sections from the anterior wall were not available, myocardial infarction was present elsewhere in these two cases.

#### SUMMARY AND CONCLUSIONS

1 The initial, early, and terminal forces associated with ventricular depolarization can be studied in greater detail and more accurately by spatial vectorcardiography than by electrocardiography.

2 The initial, early, and terminal forces are stereotyped in the normal heart, right and left ventricular hypertrophy, and right and left bundle branch block, and are altered in a characteristic way by changes in heart position and rotation. The initial and/or terminal forces help in establishing the position and degree of rotation of the heart.

3 Changes in the initial forces which cannot be explained on the basis of heart position and rotation are diagnostic of septal disease.

4 Changes in the early forces indicate infarction of the free wall of the left ventricle. Localization of infarction is established in reference to the three natural coordinate axes of the body. The abnormal vectors are oriented posteriorly and down in anterior infarction, anteriorly and down in high posterior infarction, up and posteriorly in infero-posterior wall lesions, to the left in lesions close to the interventricular septum, and to the right in lateral wall involvement. Reversal in the direction of inscription of the vectorcardiographic projections frequently results from displacement of the forces, and furnishes valuable additional help in the diagnosis of infarction. Clockwise inscription of the posteriorly placed horizontal projection is diagnostic of anterior infarction, and clockwise

inscription of the horizontally placed frontal loop is diagnostic of posterior wall infarction

5 The QRS loop is open in acute infarction, and the position of the end to the beginning of the loop is characteristic in anterior infarction, posterior infarction, acute pericarditis, and right and left ventricular hypertrophy. The T loop is long and narrow in acute, and small and round in healing or old myocardial infarction.

6 Comparison of vectorcardiographic and electrocardiographic interpretation in 50 cases studied at autopsy indicates unqualified superiority of the vectorcardiogram in the diagnosis of myocardial infarction, and right and left ventricular hypertrophy, singly or combined. The vectorcardiogram is superior for localization, and for detecting multiple areas of infarction. This superiority is evident in relation to anterior, posterior, and septal infarction. False vectorcardiographic diagnosis of infarction did not occur in this series.

7 Spatial vectorcardiography is a useful method of examination and its use should be extended.

#### RESUMEN Y CONCLUSIONES

1 Las fuerzas iniciales, precoces y terminales asociadas con la despolarización pueden estudiarse con mayor detalle y exactitud por la vectorcardiografía espacial que por la electrocardiografía.

2 Las fuerzas iniciales, tempranas y terminales están estereotipadas en el corazón normal, en la hipertrofia ventricular derecha e izquierda y en el bloqueo de ramas derecha e izquierda y son alteradas de manera característica por cambios en la posición del corazón y por la rotación. Las fuerzas iniciales y/o terminales ayudan para establecer la posición y grado de rotación del corazón.

3 Los cambios en las fuerzas iniciales que no pueden explicarse sobre la base de la posición del corazón o la rotación son diagnósticos de enfermedad septal.

4 Los cambios en las fuerzas precozmente indican infarto de la pared libre del ventrículo izquierdo.

La localización del infarto se establece en relación a los tres ejes coordinados del cuerpo. Los vectores anormales se orientan posteriormente y hacia abajo en el infarto anterior, anteriormente y hacia abajo en el infarto posterior y hacia arriba y posteriormente en las lesiones inferoposteriores de la pared, hacia la izquierda en las lesiones próximas al septum interventricular y a la derecha en el caso de daño de la pared lateral. La inversión en la dirección de la inscripción de las proyecciones vectorcardiográficas resultan a menudo del desplazamiento de las fuerzas y da valiosa información adicional en el diagnóstico del infarto. La inscripción en el sentido de las manecillas del reloj de la proyección posterior horizontalmente colocada hace diagnóstico de infarto anterior y la inscripción en el sentido del reloj del gancho frontal ubicado horizontalmente hace diagnóstico del infarto de pared posterior.

5 El gancho QRS es abierto en el infarto agudo y la posición y la

posición de su término al principio del gancho es característica en el infarto anterior, en el posterior, en la pericarditis aguda y en la hipertrofia derecha e izquierda ventriculares. La onda T es larga y estrecha en el infarto agudo y es pequeña y redonda en el infarto en curación o antiguo.

6 La comparación de la vectocardiografía y la electrocardiografía en su interpretación en 50 casos estudiados a la autopsia indica una marcada superioridad del vectocardiograma en el diagnóstico del infarto del miocardio así como en el de la hipertrofia derecha e izquierda ventriculares, ya sea simple o combinadamente.

El vectocardiograma es superior para la localización y para descubrir áreas múltiples de infarto. Esta superioridad es evidente en relación a los infartos anterior, posterior y septal. En estas series no ocurrieron falsos diagnósticos vectocardiográficos de infarto.

7. La vectocardiografía espacial es un método útil para el examen y su uso debe ser más amplio.

#### RESUME

1 Les vecteurs initiaux, précoces et terminaux qui peuvent être créés par la dépolarisation ventriculaire peuvent être étudiés avec plus de détails et plus de précision que par l'électrocardiographie par le vectocardiographie spatiale.

2 Les vecteurs initiaux, précoces et terminaux sont stéréotypés dans le coeur normal, dans l'hypertrophie du ventricule droit et gauche, dans les blocs de branches droits et gauches, et sont modifiés d'une façon caractéristique lors de modifications de la position du coeur et lors de sa rotation. L'étude des vecteurs initiaux et terminaux peut aider à établir la position et le degré de rotation du coeur.

3 Les modifications des vecteurs initiaux qui ne peuvent être expliquées par des questions de position ou de rotation cardiaque permettent de diagnostiquer une lésion septale.

4 Les altérations des vecteurs précoces sont la preuve d'un infarctus de la paroi libre du ventricule gauche. La localisation de l'infarctus s'établit en fonction des trois coordonnées normales du corps. Les vecteurs anormaux sont orientés en arrière, et en bas, dans les infarctus antérieurs, en avant et en bas dans les infarctus postérieurs haut situés, en haut et en arrière dans les lésions de la paroi inféro-postérieure. Ils sont orientés vers la gauche dans les lésions qui sont proches du septum interventriculaire et vers la droite sur les altérations de la paroi latérale. Des inversions de la direction d'inscription de la projection vectocardiographique sont les résultats fréquents du déplacement des vecteurs et sont un auxiliaire précieux dans le diagnostic d'infarctus. La rotation horaire de la projection vectocardiographique horizontale, placée en arrière traduit le diagnostic d'infarctus antérieur et la rotation horaire de l'onde frontale placée horizontalement traduit le diagnostic d'infarctus de la paroi postérieure.

5 L'onde QRS est ouverte dans l'infarctus en phase aiguë et sa position de la terminaison au commencement est caractéristique dans l'infarctus antérieur, l'infarctus postérieur, la péricardite aiguë, l'hypertrophie ventriculaire droite et gauche. L'onde T est longue et étroite dans l'amélioration brusque, temporaire et rapide, ou dans un infarctus myocardique ancien.

6 La comparaison de l'interprétation vectocardiographique et électrocardiographique dans 50 cas étudiés à l'autopsie montre la remarquable supériorité du vectocardiogramme dans le diagnostic d'infarctus myocardique, d'hypertrophie ventriculaire droite et gauche, simple ou associée. Le vectocardiogramme est supérieur à l'électrocardiogramme pour diagnostiquer les localisations et les multiples zones d'infarctus ainsi qu'en ce qui concerne l'infarctus antérieur, postérieur et septal. Dans la série de cas étudiés, il n'y a pas d'erreur de diagnostic vectocardiographique pour l'infarctus.

7 La vectocardiographie spatiale est un procédé d'examen utile et dont l'emploi devrait être étendu.

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# The Ventricular Pulsations in Myocardial Infarction; a Fluoroscopic and Kymographic Study

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The study of left ventricular contraction by fluoroscopy,<sup>1</sup> roentkymography,<sup>2, 3</sup> and electrokymography<sup>4, 5</sup> has proved to be of great practical value in the detection of myocardial disease, particularly myocardial infarction. Visualization and analysis of the left ventricular border movements should be part of every routine cardiac fluoroscopy, affording a simple and accurate method for detecting localized areas of myocardial disease which is readily available in the office and clinic. For more detailed study and analysis of left ventricular border pulsations than can be attained by fluoroscopy one can utilize the electrokymograph or roentgenkymograph which are available in the clinic and hospital.

## *Normal Left Ventricular Contraction*

Fluoroscopic observation of the cardiac pulsations in normal individuals reveals uniform inward or medial movement of the entire left ventricular border during systole (Fig 1). The timing of the ventricular border movements can be checked by comparison with those of the aortic knob. The latter segment moves laterally and expands during ventricular systole as a result of aortic filling. Thus, there is a seesaw movement of the left cardiac border about the middle segment in the region of the left auricular appendage ("point of no motion"). The upper arterial segment, comprising the pulmonary artery and aorta, expands during systole and moves outward and laterally. The left ventricular segment below it contracts during systole and moves inward or medially. Although the inward movement of all points along the left ventricular border is not entirely simultaneous it is fairly uniform. The upper part of the left ventricular border moves inward and downward, the middle or supra-apical part moves inward and medially and the lower or diaphragmatic segment moves inward and upward.

The left ventricular movements can be studied also in the slight left and right oblique views. In general, the character of the ventricular pulsations in the oblique views is similar to that of the P-A view. In the left oblique view, however, the movements may be rotatory or spiral in character and the inward or medial movement may be preceded by a transient outward expansile movement at the onset of systole. Electrokymography has demonstrated that these variations are due mainly to positional factors affecting the border movements.<sup>5, 7</sup>

Electrokymography is a graphic method for recording the cardiac pulsations<sup>7, 8</sup> and is based on the use of a photosensitive multiplier tube which is attached to the ordinary fluoroscopic screen. When the position of the tube is adjusted so that the slit lies over the heart border to be studied,

the movements of the border produce cyclic variations in the intensity of fluorescent light entering the photo-tube. This is transformed into a pulsating flow of electrons which is amplified and recorded as a phasic curve by a galvanometer, simultaneously with other reference tracings such as the carotid pulse and the heart sound tracings. The polarity of the apparatus is such that downward movement of the electrokymographic curve represents inward or medial movement of the underlying heart border, and upward movement of the curve represents outward or lateral movement of the underlying border.

The electrokymogram obtained from the left ventricular border has a characteristic appearance (Fig 2). In general, it resembles a ventricular volume curve with superimposed positional movements at the onset of systole and diastole. A typical curve shows a steep downward limb during systole, representing inward or medial movement of the left ventricular border during the ejection phase. This may be preceded by a small transient upward movement lasting 0.02 to 0.06 second, which is generally due to a positional movement or change in shape of the heart at the onset of ejection. During the isometric phase preceding ejection, the curve may show a horizontal segment or a slight upward or downward movement.

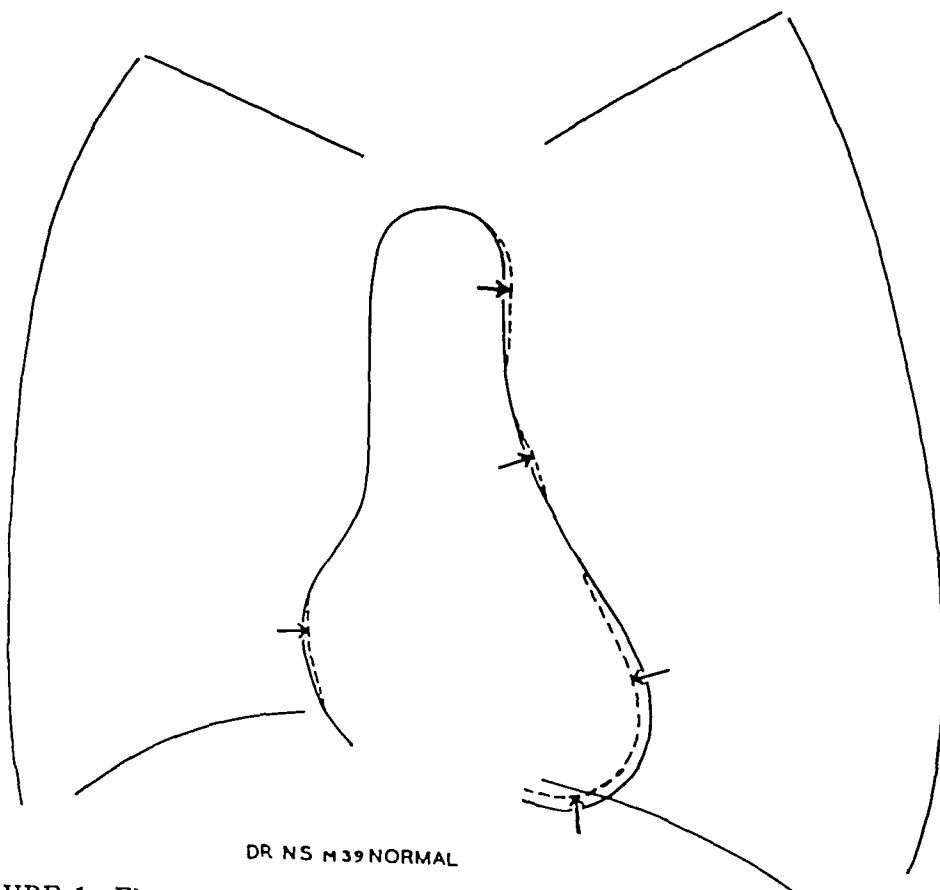


FIGURE 1 Fluoroscopic appearance of the cardiac borders in systole and diastole of a normal individual as traced from the fluoroscopic screen. The arrows indicate the direction of border movement during systole. The aortic and pulmonary artery segments move outward during systole while the left ventricle border moves inward.

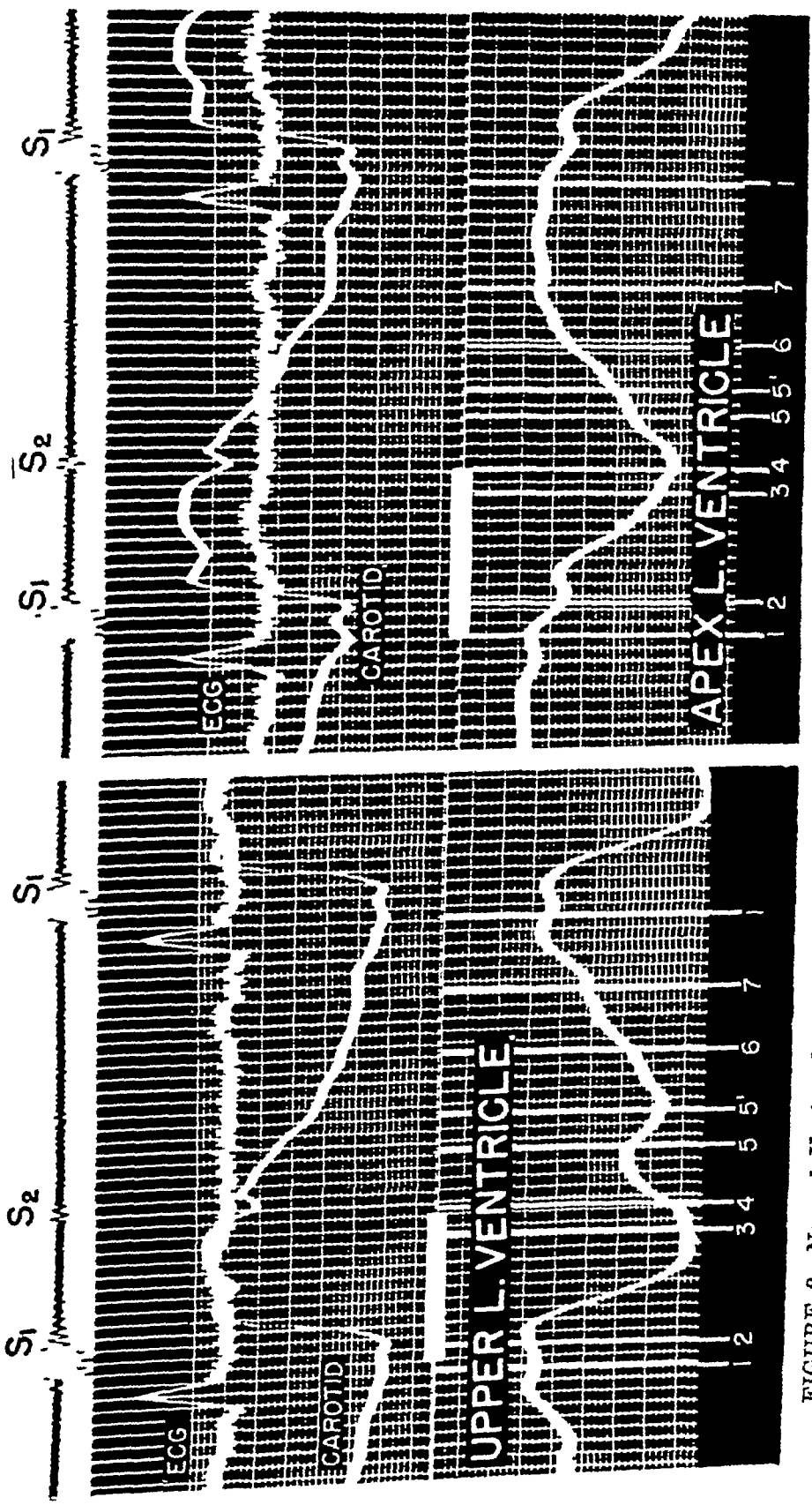


FIGURE 2 Normal Ventricular Electrocardiograms. Electrocardiograms of the upper and apical segments of the left ventricular border of a normal individual, recorded simultaneously with the phonocardiogram, electrocardiogram and carotid pulse tracing. Downward and upward movements of the electrocardiogram indicate inward and outward movements of the ventricular border, respectively. The ventricular curve may be subdivided into the following phases of the cardiac cycle: isometric contraction (1-2), ejection (2-3), protodiastole (3-4), isometric relaxation (4-5), rapid filling (5-6), slow filling (6-7). The differences in configuration of the two curves are due to positional movements of the heart at the onset of systole and diastole.

lasting for 0.02 to 0.04 second. The steep downward movement of the ejection phase is succeeded by a V-shaped or horizontal segment, representing the isometric relaxation phase. This is then followed by upward movement of the curve during ventricular diastole and filling, which is fairly steep in its early portion (rapid inflow phase) and shallower in its late portion (slow inflow phase).

### *Ventricular Pulsation in Myocardial Infarction*

Myocardial infarction produces characteristic abnormalities of left ventricular contraction which can be recognized visually during routine fluoroscopy<sup>1</sup> and recorded graphically by the roentgenkymograph<sup>2, 3</sup> and electrokymography<sup>4-6, 9</sup>. These abnormalities of left ventricular contraction can be detected during systole and diastole.

The abnormalities of the systolic phase may be classified in three main groups: 1. Localized diminution or absence of ventricular pulsation; 2. Partial reversal of pulsation during early systole; 3. Complete reversal of pulsation or paradoxical ventricular movement.

*Localized Diminution or Absence of Ventricular Pulsation.* In this abnormality there is observed during fluoroscopy a lack of movement localized to one segment of the left ventricular border (Fig. 3 and 4). This generally involves the lower half or apical region of the left ventricular border. Electrocardiographic curves obtained from the involved segment

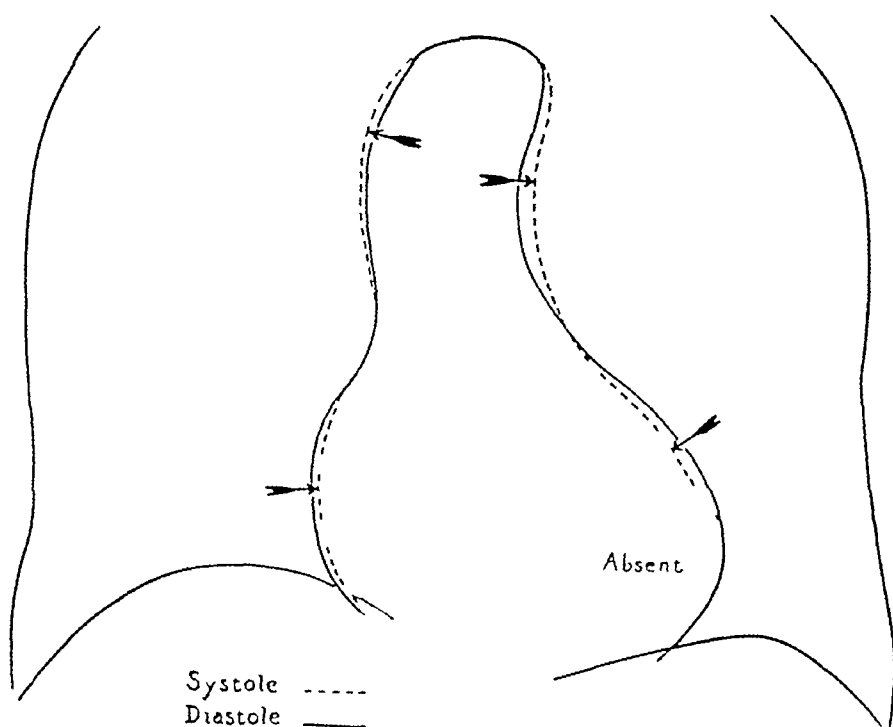


FIGURE 3. Localized absence of left ventricular pulsation observed fluoroscopically in a patient with previous myocardial infarction 4 years ago. During systole there is absence of inward movement of the lower third of the left ventricular border in contrast to normal pulsation of the upper left ventricular border and aorta.



show marked diminution in amplitude and even absence of the systolic and diastolic waves

To be significant the diminished amplitude of pulsation should be localized to one segment of the left ventricular border rather than involve the entire cardiac border. Also, diminished movement of the left ventricular border just above the diaphragm in obese patients or of the apical segment when it is obscured by a pericardial fat pad should be interpreted with caution. This abnormality probably results from impairment of left ventricular contraction which is not severe enough to produce actual ballooning out of the ventricular wall or reversal of pulsation during systole.

*Reversal of Left Ventricular Pulsation (Paradoxical Movement)* In this abnormality the involved segment of the left ventricular border balloons out during systole. This may be a transient phenomenon at the onset of systole following which it is succeeded by a delayed inward movement (partial reversal of pulsation) or it may be sustained for the entire duration of systole (complete reversal of pulsation).

Fluoroscopically, reversed or paradoxical pulsation is visualized as an outward movement of a segment of the left ventricular border, generally the middle or apical segment (Fig 5). As the uninvolved upper segment of the left ventricular border moves inward or medially during systole (timing checked with the aorta and pulmonary artery) the lower segment moves outward and laterally. Thus, there is a seesaw movement over

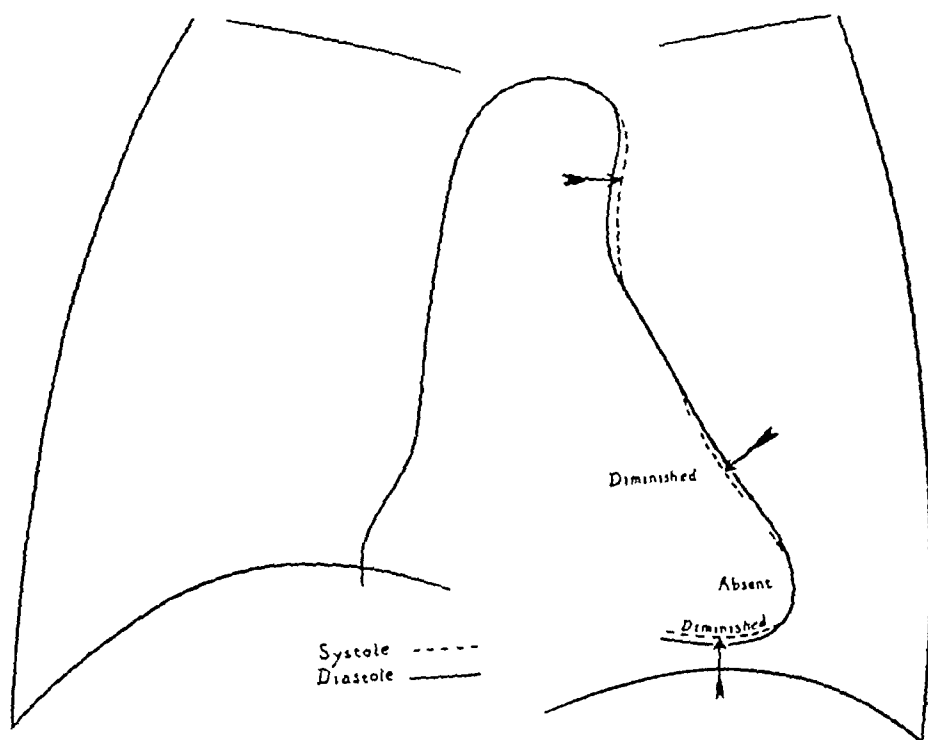


FIGURE 4 Localized absence of left ventricular pulsation observed fluoroscopically in a patient with previous myocardial infarction one year ago. The upper segment of the left ventricular border moves inward during systole and the inferior or diaphragmatic segment moves inward and upward. However, the apical segment fails to contract.

the left ventricular border. The involved weakened segment of the left ventricular border is ballooned out or actually thrust out as the remaining uninvolved border contracts and moves inward. In some cases there is a wavy motion over the left ventricular border and in other cases there may be a double pulsation during systole.

In the electrokymogram, reversed or paradoxical left ventricular pulsation is manifested by upward movement of the curve which generally begins during the isometric phase of systole or at the onset of the ejection phase. This is sustained for a variable period of time, depending on whether the reversal is partial or complete. In partial reversal, the upward systolic movement is replaced in early or mid systole by inward movement which may be normally steep or abnormally retarded (Figs 6 and 7). The upward movement generally lasts for more than 0.08 second. This differentiates it from a positional movement which may occur in a normal heart but the duration of which is less than 0.08 second.

In complete reversal of pulsation the upward movement of the curve is sustained for the entire duration of systole and is followed by a collapse of the curve at the onset of diastole (Figs 8 and 9). The latter generally occurs during or at the end of the isometric relaxation phase. The resulting curve is completely paradoxical and resembles an arterial curve instead of a normal ventricular curve (Fig 10).

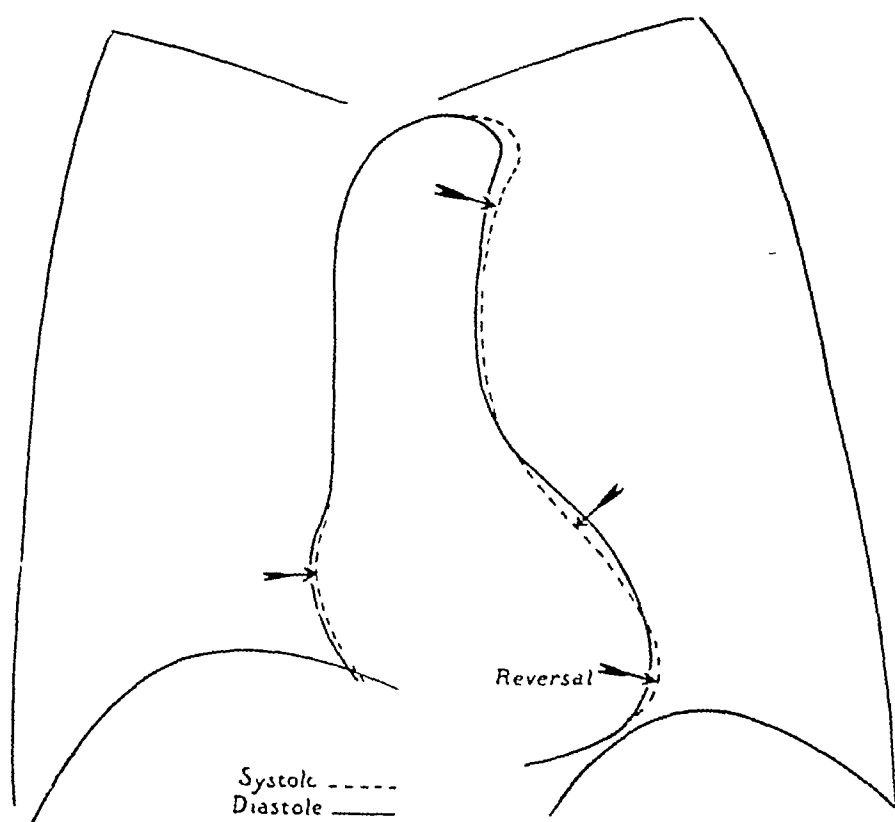


FIGURE 5 Reversal of left ventricular pulsation observed fluoroscopically in a patient with previous myocardial infarction three months ago. There is paradoxical pulsation of the lower half of the left ventricular border which moves outward during systole as the upper left ventricular border moves inward.

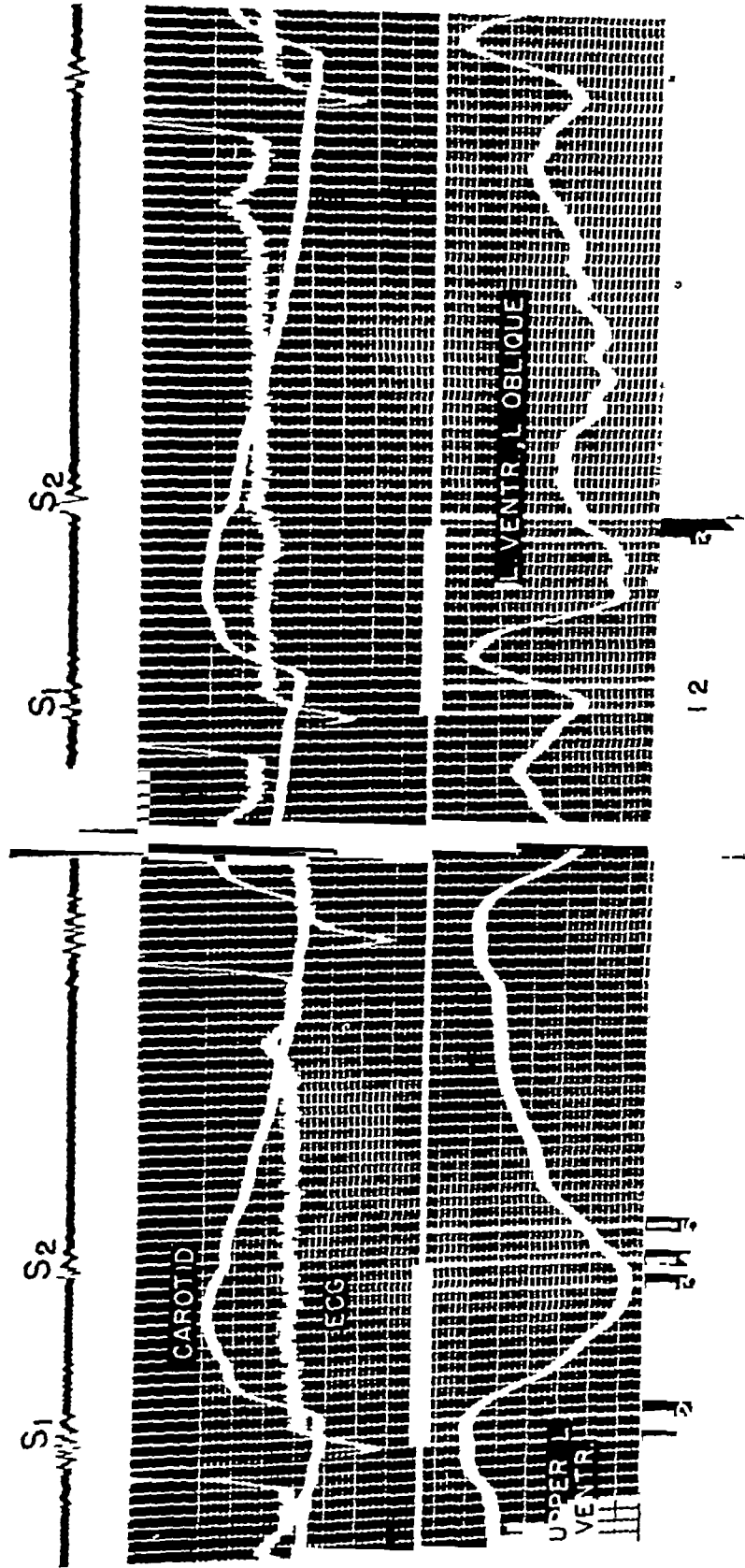


FIGURE 6 Electiokymograms showing partial reversal of pulsation of left ventricular border in a patient with previous myocardial infarction two years ago. The upper left ventricular border electiokymogram is normal. The curve recorded from the left ventricle in the left oblique view shows upward movement at the onset of systole which is sustained for approximately 0.12 sec (each vertical line represents 0.02 sec). There is marked diminution of pulsation during the remainder of the cardiac cycle. In this case the abnormal ventricular pulsation was observed and recorded only in the left oblique position. The ECG findings were obscured by bundle branch block.

*Incidence of Abnormal Ventricular Contraction* Previous studies<sup>1, 2, 3</sup> of a large series of patients with proven myocardial infarction have indicated that partial or complete reversal of left ventricular pulsation occurs in approximately 50 to 60 per cent of patients, localized diminution or absence of pulsation in 20 to 25 per cent and normal pulsations in the remainder. These statistics were derived from fluoroscopic observation, electrokymography and roentgenkymography. Of course, the incidence of abnormal pulsation would be expected to be higher when the graphic methods are employed, owing to the objectivity of these methods, particularly electrokymography. For example, a slight reversal of pulsation may be missed during fluoroscopy but would be easily demonstrated when magnified approximately 20 times by the electrokymogram. On the other hand, a false positive diagnosis of reversed pulsation is occasionally made from fluoroscopy alone. In our experience, however, a well-trained fluoroscopist, who is aware of the abnormalities which occur following myocardial

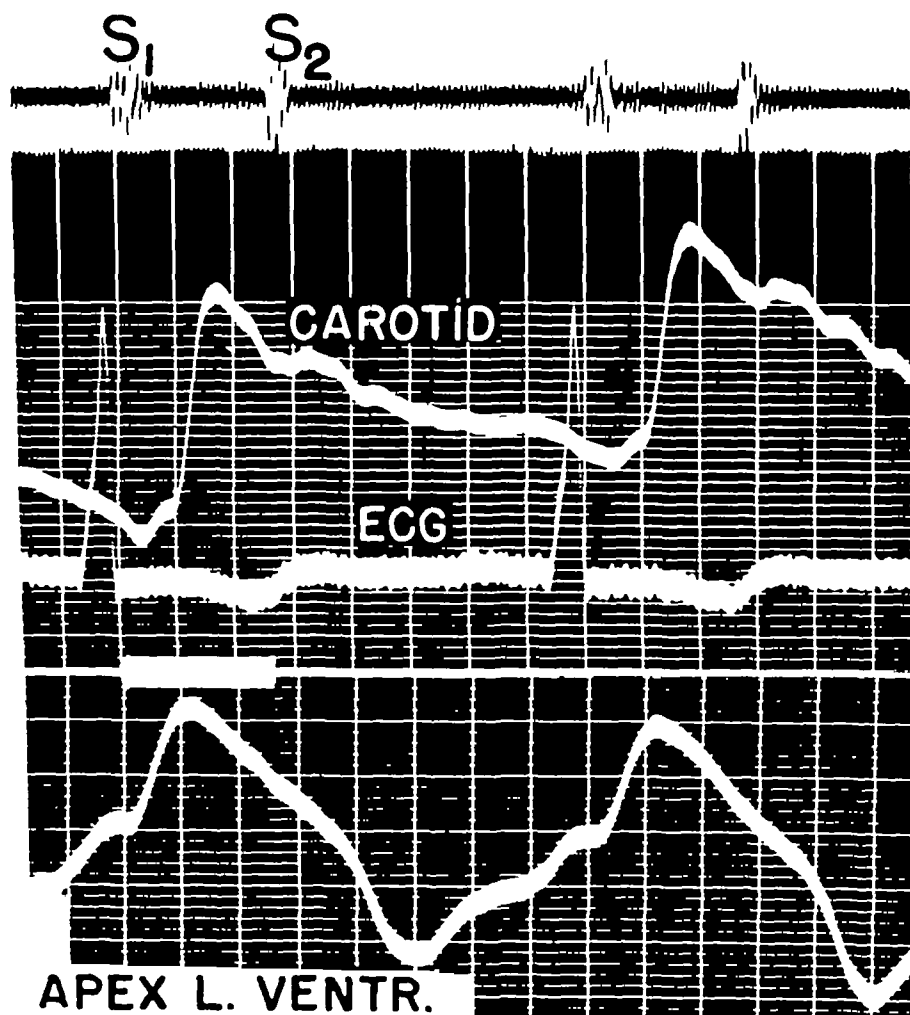


FIGURE 7 Electrocardiogram of apex of left ventricular border in a 28 year-old man with aneurysmal dilatation of the left ventricle due to obscure congenital myocardial disease. The curve moves upward during early systole and shows delayed downward movement during late systole and early diastole. This is a partial reversal of pulsation and indicates impaired left ventricular contraction.

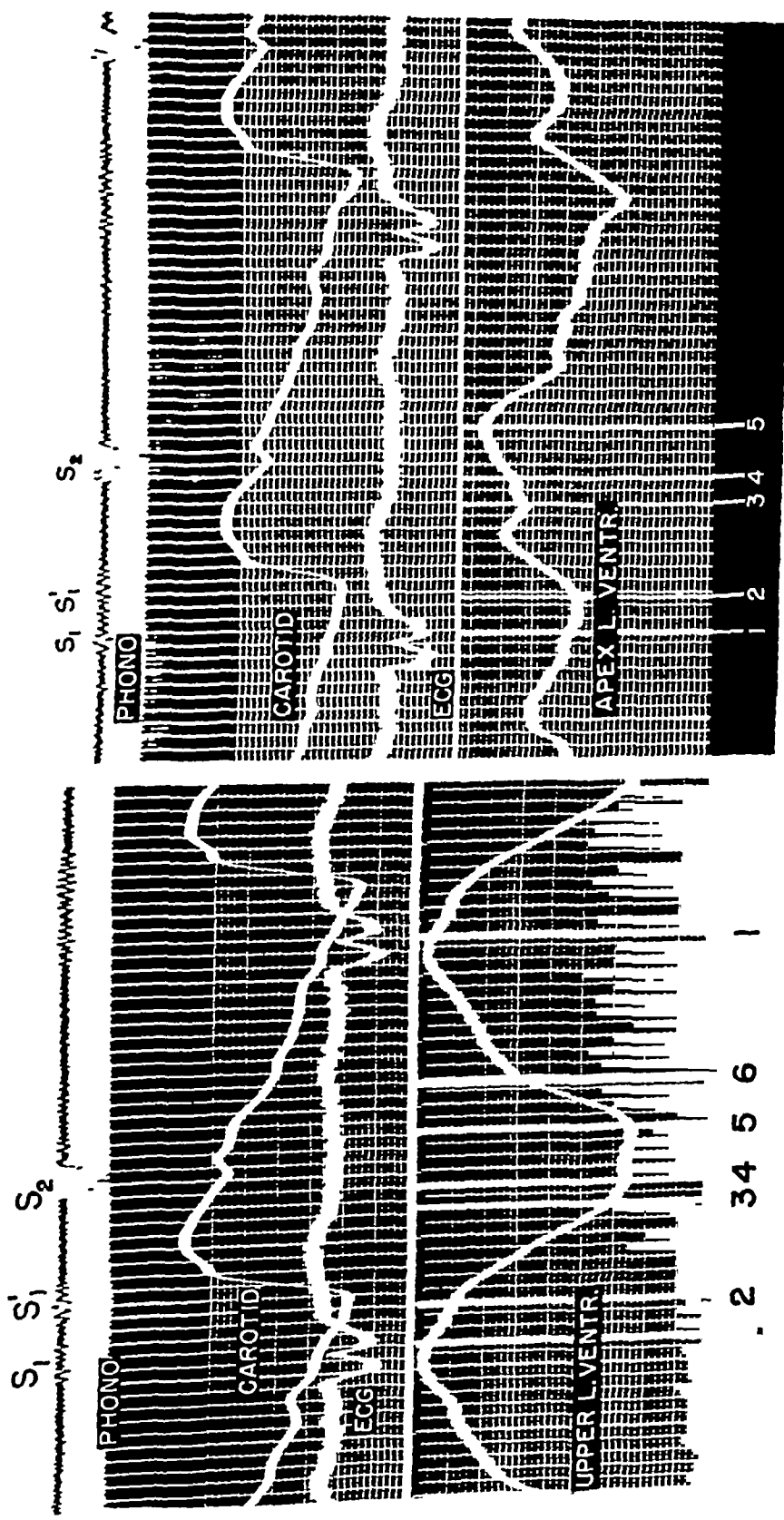


FIGURE 8 Electokymograms showing complete reversal of left ventricular pulsation in a patient with previous anterior wall infarction three months ago. The upper left ventricular border movement is normal. The curve of the apical segment shows upward movement which is sustained for the entire duration of ventricular systole. This is a paradoxical curve and is pathognomonic of myocardial infarction.

infarction and who looks for them routinely, can become almost as accurate in visualizing the abnormal movements by fluoroscopy as with the graphic method. It is only when the ventricular movements are markedly diminished in amplitude, particularly in the presence of a markedly dilated heart, that the fluoroscopist may have difficulty in establishing the presence or absence of paradoxical movement in addition to the diminished movement. It is in this type of case that electrokymography attains its greatest practical clinical value as a diagnostic tool.

*Location of Abnormal Ventricular Movements* The most frequent site of abnormal pulsation in myocardial infarction is the lower half or third of the left ventricular border. Not infrequently in a large infarct the reversal involves almost the entire ventricular border with only a small upper segment below the left auricular appendage which is uninvolved. On the other hand, reversed pulsation is occasionally limited to the middle or upper segment of the left ventricular border, with normal pulsation below this area (Fig 10). In other cases the reversal is limited to the apical region just above the diaphragm. In sthenic individuals or in the presence of left ventricular hypertrophy the apex may be covered by the diaphragm and the abnormal ventricular pulsation is exposed only during a deep inspiration. In such a case one must guard against the patient straining while he holds his breath since he may perform the Valsalva maneuver which may result either in marked diminution in amplitude of pulsation or occasionally in reversed pulsation even in the absence of heart disease.

In the majority of cases the abnormal left ventricular pulsations are visualized or recorded in the P-A view. This holds true regardless of the location of the infarction as determined by the electrocardiogram.<sup>8</sup> In other words, whether the infarction is located on the anterior, lateral or diaphragmatic surface of the left ventricle, the abnormal movement is observed in the P-A view. Not infrequently, however, rotating the patient into a very slight left or right oblique view (5 to 15°) may accentuate the abnormal border movement (Fig 6). Thus, in anterior infarction reversal of pulsation may be more readily visualized at the apex when the patient is rotated very slightly into the right anterior oblique rotation. In posterior infarction reversed pulsation may be visualized in the slight left oblique view as well as in the P-A view. It is only in the occasional case of posterior or diaphragmatic wall infarction that reversed pulsation is observed only in the left oblique view and not in the P-A view.

*Onset and Duration of Abnormal Ventricular Pulsation* It is difficult to ascertain the exact time of appearance of absent or reversed ventricular pulsation following clinical myocardial infarction since patients with acute infarction are not generally fluoroscoped or examined kymographically during the acute stage. However, our studies<sup>2</sup> with serial roentgenkymograms have suggested that the abnormal pulsation is often present during the first week following the clinical attack and almost always has developed by the second week of the attack. Not infrequently it begins as

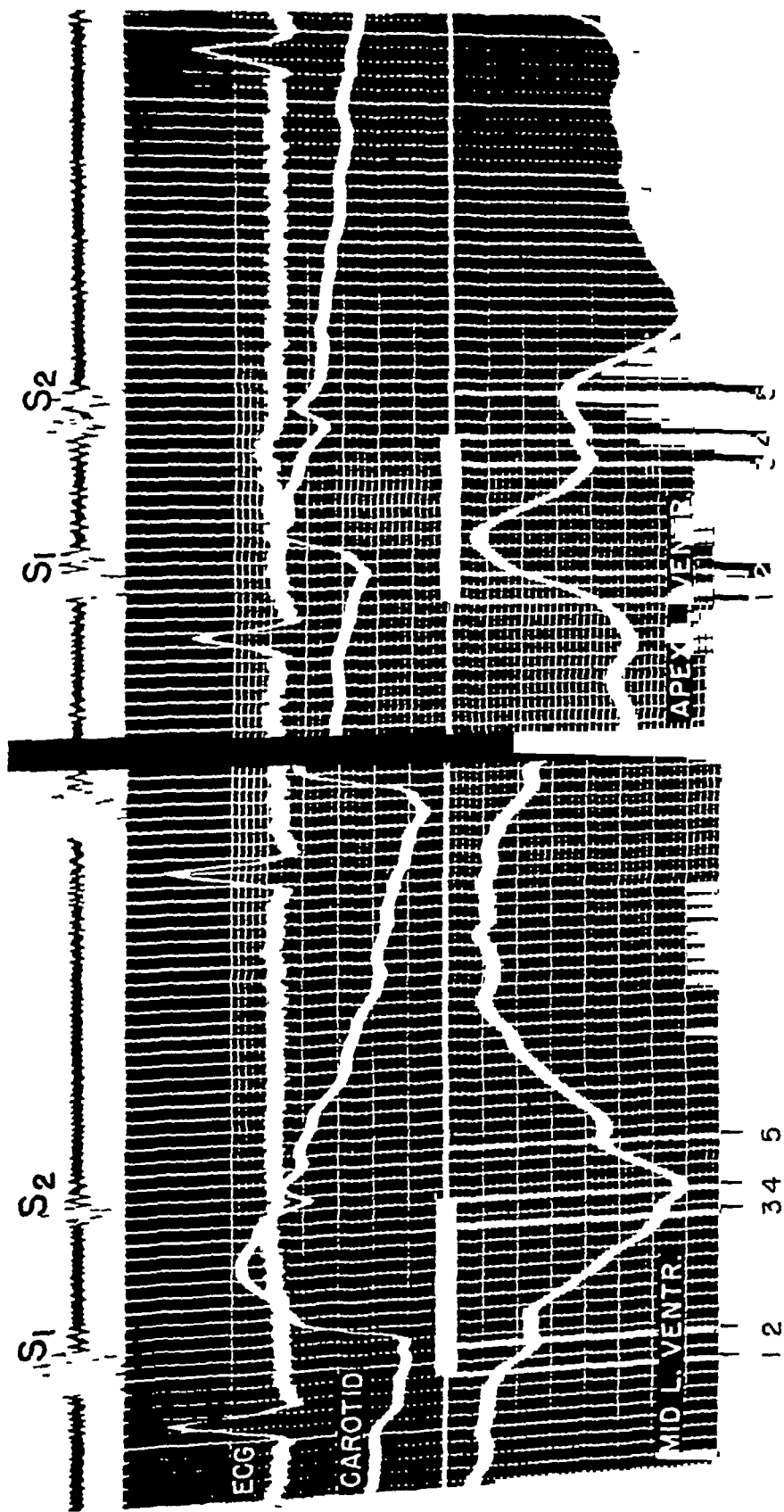


FIGURE 9 Electrocardiograms of left ventricular border showing almost complete reversal of pulsation in a patient with previous anterolateral myocardial infarction four years ago. The curve obtained from the mid left ventricular segment is fairly normal. At the apex the curve is paradoxical showing marked upward movement which is sustained during the first half of systole. The curve shows a further fall at the end of systole and almost complete absence of filling movement during diastole.

a localized diminution or absence of pulsation which progresses to partial or complete reversal of pulsation

Absent or reversed ventricular pulsation is often permanent. In a small percentage of cases it may disappear entirely or become less marked. In the great majority of cases, however, it lasts for many years. This may be of great diagnostic importance since the abnormal pulsation may persist even when the patient makes a complete clinical recovery and even if the electrocardiogram becomes normal or if the typical findings of myocardial infarction disappear.<sup>3</sup> In such a case, reversal of pulsation, visu-

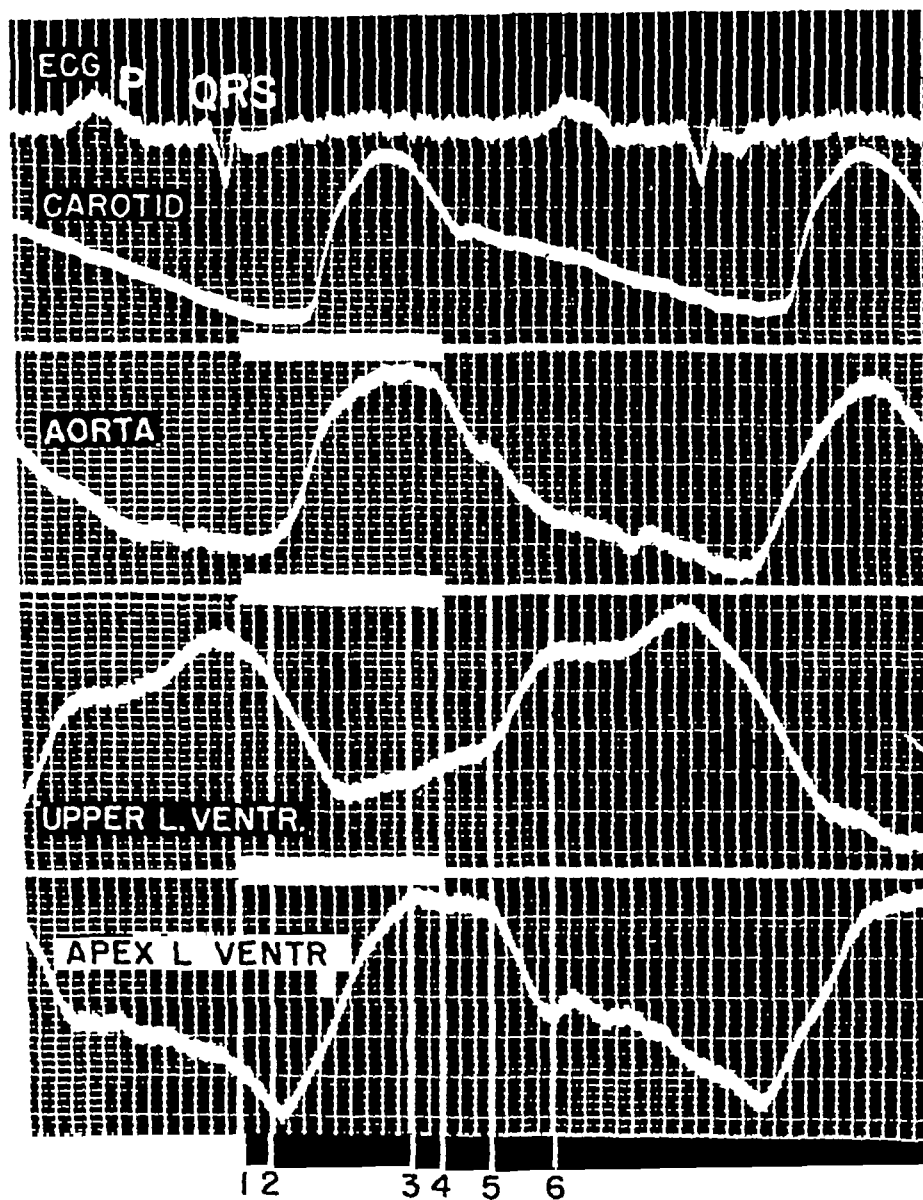


FIGURE 10 Electrokymograms of left ventricular border of patient with aneurysm of the left ventricle due to old myocardial infarction. The curve of the upper left ventricular border is normal. The curve of the apical segment is completely paradoxical, resembling the arterial curve of the aorta. There is upward movement of the curve which is sustained throughout systole and then falls in early diastole (5-6).



alized by fluoroscopy or recorded kymographically, may be the only residual finding indicative of previous myocardial infarction

*Differential Diagnosis of Reversal of Pulsation* As already stated, reversal of pulsation, particularly the partial type which is of short duration and limited to the early phase of systole (Fig 6), must be differentiated from the transient outward movement of the left ventricular border observed in normal individuals which is of positional origin (Fig 2) The latter is generally short in duration and rarely exceeds 0.06 second Early reversal of pulsation lasts for at least 0.08 second and generally exceeds this duration

Fluoroscopically, it may be difficult to differentiate early reversal of pulsation from a physiological outward movement This may explain the occasional erroneous fluoroscopic diagnosis of myocardial infarction in an apparently normal individual If the transient outward movement is observed over the entire left ventricular border the probability exists that it represents a physiological outward movement Electrocardiography, of course, may be the only accurate method to make this important differentiation

The occurrence of an early physiological outward movement of the left ventricular border may be the result of several factors<sup>9</sup> It may be due to a traction movement of the heart on the great vessels at the onset of contraction which produces a positional movement of the heart borders superimposed on the contractile movements of the various chambers Secondly, it may be due to a change in the shape of the heart which has been demonstrated to occur in the early part of systole This is caused by early unopposed contraction of the intraventricular septum before contraction of the free wall of the ventricle, leading to shortening of the heart in its longitudinal axis and transitory bulging outward of the free walls. This is cut short when the free walls contract and the heart borders move inward

*Physiologic Basis for Reversed Pulsation* Since the experiments of Tennant and Wiggers,<sup>10</sup> it is well known that following ligation of a coronary artery in the dog the ischemic portion of the myocardium ceases to contract within one minute and then begins to balloon out as the remainder of the ventricle contracts The rise in intraventricular pressure at the onset of systole expands the weakened wall of the ischemic ventricular segment which collapses at the end of systole when the intraventricular pressure falls

There is a close similarity of these events following experimental coronary ligation to those observed following clinical coronary occlusion except that it may take several days for the abnormal contraction to appear Paradoxical left ventricular movement following myocardial infarction indicates the presence of a weakened area or scar in the ventricular myocardium which either fails to contract and remains motionless during systole or is ballooned out by the rising intraventricular pressure

Several factors are responsible for the magnitude, extent and persistence

of the abnormal ventricular movement. These include the size and location of the infarcted area, the degree of healing and contraction of the resulting scar and the state of the collateral circulation. Experimental ballooning of the left ventricular wall following coronary ligation may be temporary or may be abolished by the release of the ligature or it may disappear spontaneously if the ligated vessel and resultant ischemic area are small<sup>10, 11</sup>. It may be increased in extent or magnitude by reducing the blood pressure to shock levels whereas restoration of normal blood pressure and reduction of coronary insufficiency results in complete or partial disappearance of the myocardial ballooning<sup>12</sup>.

From a physiologic standpoint every myocardial area of infarction associated with reversed or paradoxical pulsation acts dynamically as a ventricular aneurysm, despite the fact that radiological examination of the heart usually fails to show any localized bulge of the left ventricular border. Since the ballooning out of the ventricular wall occurs only in systole, it cannot be demonstrated by the conventional roentgenogram unless it is exposed only during systole, but has been strikingly demonstrated by cinematography of the heart. By this method a localized bulge of the left ventricular border is visible only in the frames exposed during ventricular systole and it disappears during diastole. When a typical aneurysmal bulge is visible on the roentgenogram, fluoroscopic examination or electrokymography will almost always demonstrate complete absence or reversal of ventricular pulsation over the involved segment as in any infarcted area of large extent (Fig 10).

If the explanation is correct that reversed pulsation is due to ballooning of a weakened segment of the left ventricular wall, it is difficult to explain the frequent lack of correlation of the location of the abnormal movement and the actual site of infarction. It has been mentioned previously that irrespective of the actual site of infarction, the most common location of the abnormal ventricular movement is the apical segment of the left ventricular border in the P-A view, which may be at some distance from the infarcted area. The explanation for this is unknown. In previous publications<sup>1, 2</sup> it was speculated that it may be related to the spiral arrangement of the cardiac muscle bundles which wind around the apex of the heart from the base and are attached into the valve rings. It is possible that the muscle bundles act as a fulcrum, the weakening of any portion of this fulcrum whether anterior or posterior may result in ballooning out of the apical region.

#### SUMMARY

Cardiac fluoroscopy and kymography give important information in the study of the patient with myocardial infarction. The observation of marked localized diminution of pulsation of the left ventricular border or of complete or partial reversal of pulsation is indicative of a circumscribed area of myocardial damage, usually as a result of previous myocardial infarction. Such findings may be observed in the absence of other typical clinical findings of previous myocardial infarction. Careful exami-

nation of left ventricular border motion should be a routine part of every chest fluoroscopy

The incidence, location, duration, clinical significance, differential diagnosis and physiologic basis for abnormal left ventricular motion in myocardial infarction is reviewed

### RESUMEN

La fluoroscopia y la kimgrafia cardiacas dan información importante para el estudio del enfermo de infarto miocárdico. La observación de una marcada disminución de la pulsatilidad en área localizada del borde del ventrículo izquierdo o bien la observación de una inversión completa o parcial de esa pulsatilidad, indican una área circunscrita de daño del miocardio, generalmente como resultado de un infarto previo. El examen cuidadoso de la motilidad del borde ventricular izquierdo, debe ser una parte rutinaria de toda fluoroscopia del tórax. Se hace una revisión de la incidencia, ubicación, duración, significación clínica, diagnóstico diferencial y bases fisiológicas de la motilidad anormal del ventrículo izquierdo en el infarto del miocardio.

### RESUME

La radioscopie du coeur et la kymographie apportent des renseignements importants pour l'étude des malades atteints d'infarctus du myocarde. La constatation d'une zone où les pulsations sont nettement moins marquées sur le bord du ventricule gauche, ou la perception d'inversion complète ou partielle des pulsations, indique qu'il existe une zone circonscrite de lésions myocardiques. Dans ce cas, il s'agit généralement de la conséquence d'un infarctus myocardique antérieur.

De telles constatations peuvent être faites alors qu'il n'y a aucun autre signe clinique manifeste d'un infarctus myocardique antérieur. L'examen attentif des mouvements du ventricule gauche devrait être un élément de routine lors de tout examen radioscopique du thorax.

L'auteur étudie la fréquence, la localisation, la durée, la valeur clinique, le diagnostic différentiel et les bases physiologiques des mouvements anormaux du ventricule gauche dans l'infarctus du myocarde.

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# Remarks on the Graphic Diagnosis of Coronary Disease

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## *I. Typical and Atypical Electrocardiograms in Myocardial Infarction Caused by Acute Coronary Occlusion and Coronary Insufficiency*

The electrocardiogram has been epic making in the diagnosis of coronary occlusion and is the main reason for the ever increasing frequency with which this disease is detected. The ordinary electrocardiographic diagnosis has become so well-recognized that it is now well to talk, not only of the typical electrocardiogram, but of the atypical electrocardiogram in myocardial infarction. It is time also to divide the study of myocardial infarction into two types, (1) the subendocardial type, secondary to coronary insufficiency, that is, without complete occlusion of a coronary artery, (2) the through-and-through type caused by coronary occlusion, that is, complete obstruction of a coronary artery. Coronary insufficiency is usually associated with coronary sclerosis but may be observed in a normal heart, for example, following hemorrhage. In coronary insufficiency the electrocardiogram shows RS-T depression, T-wave inversion, or RS-T depression and T-wave inversion combined, since the damage is localized in the subendocardial region. For the same reason, the outlook is much better in coronary insufficiency. The electrocardiographic alterations are usually transient, lasting a day or two, or one or two weeks or months, rarely they are permanent. The T-wave inversions are not usually as deep as those seen in coronary occlusion. There are no Q-waves or RS-T segment elevations because there is no through-and-through infarction. It may take a few days for the electrocardiographic changes to develop, hence, if an acute coronary episode of any kind is suspected the electrocardiogram should be repeated several times.

The type of electrocardiogram just described, that is, with RS-T depressions and T-wave inversions, but without deep Q-waves, is also seen in the premonitory phase of a coronary occlusion. Obviously there is a partial occlusion which causes coronary insufficiency. I believe that, once the artery is completely occluded, the clinical and electrocardiographic picture of coronary occlusion appears, that is, RS-T elevation is seen immediately. Within the first 12 to 24 hours the characteristic deep Q-wave is not seen but one can almost discern it if he looks intently. After 12 to 24 hours it is usually quite obvious. In anterior wall infarction the deep Q and RS-T elevations appear in leads I, aVL and in chest leads. In diaphragmatic or inferior wall infarction these alterations appear in leads II, III and aVF. In true "posterior" infarction, tall R-waves appear on the right side of the chest, i.e., in  $V_1$  and  $2$ . Q-waves may be seen in  $V_5$ ,  $6$ ,  $7$  or  $V_8$ .

Doctor Jaffe has been in the forefront in the description of atypical changes in coronary occlusion. For example, in serial electrocardiograms, temporary improvement may occur.

I personally feel that after complete occlusion the electrocardiogram will show the typical Q and RS-T patterns in 95 to 97 per cent of the cases. It does seem that, rarely, deep T-waves alone are present. In these cases there is enough normal muscle in the subepicardium to prevent the appearance of Q-waves.

## *II Cardiac Diagnostic Methods in Coronary Artery Disease Electrocardiogram, 2-Step Exercise Test and Ballistocardiogram*

The "2-step" exercise electrocardiogram has become a diagnostic means for demonstrating coronary disease in the presence of a normal resting electrocardiogram, if the resting electrocardiogram is abnormal there is, of course, no need for performing the "2-step" test. My co-workers and I feel strongly that in the presence of definite coronary disease, the "2-step" test, either the single or the double, is positive in 95 per cent of the cases. Also, when the double "2-step" test is negative, coronary disease is excluded in 95 per cent of the cases, of course not in every case. However, when one speaks of a positive "2-step" test alone, without knowledge of the clinical story, one is in an insecure position. A positive "2-step" test should not be given any significance unless the clinical story is known. There is a small percentage of normal people who show positive tests, the so-called "false" positives, and also many people with an anxiety state do this. Hence, to diagnose "coronary" disease on a positive "2-step" electrocardiogram without clinical data or correlation, is not sound.

Another point that must be mentioned is the need for standardization in the performance of the Master "2-step." The exertion must be standardized for age and weight. The heavier a person, the more work he does and the fewer trips are required. The older the patient, the less stamina he has and again fewer trips will be "normally" made. The test does not depend on previous training—it depends on age, weight and the state of the coronary circulation.

There have been numerous "modifications" of the Master "2-step" test. If the patient is walked until pain appears, if he is asked to "run up" a flight of stairs, if he squats and stands alternately, if he hops on one foot, or any other type of exercise is used, it is not the test that my colleagues and I have described. For example, every "accident" following an exercise test that we have investigated occurred after some test other than the "2-step" test. We have been fortunate, indeed, that in a score of thousands of cases under the supervision of my colleagues and myself, we have never had an accident. First, the test should never be done unless the resting 12-lead electrocardiogram is negative, secondly, if coronary disease is suspected, the single test should be done first, only if this is negative should the double test be performed. If the patient is considered to be acutely ill, it goes without saying that the test should not be done.

We have, we hope, decreased the number of "false" positives by having the tests performed essentially the way a basal metabolism is taken. The patient comes in the morning after a good night's rest, he has no breakfast or, at the most, a light breakfast. He is not permitted to smoke. He is rested a little while on arriving at the office.

In regard to the *ballistocardiogram*, I think the day will come when it will be a more scientific instrument. With physicists and mathematicians working on the machine, trying to improve it, to standardize it, to simplify the technique, I believe that we have a great deal to hope for in the ballistocardiogram. At the present time, however, we must admit that a positive test is observed in hypertension, frequently in apparently normal people over 50, and in people with peripheral vascular disease without heart disease.

There is no specific ballistocardiographic pattern of any type of heart disease although a small "k" has been described in aortic stenosis, coarctation of the aorta and in shock with diminished blood volume in the aorta and its branches. In mitral stenosis, notching of the "k" has been reported. In emphysema the ratio of the inspiratory size of the I-J wave to the expiratory I-J is changed and has been used diagnostically.

An abnormal ballistocardiogram in persons under the age of 50 should be given consideration but it must be correlated with the clinical picture as a whole. Thus, a positive "2-step" exercise electrocardiogram adds weight to the importance of the ballistocardiogram and, in fact, it works both ways.

### *III The Vectorcardiographic Diagnosis of Myocardial Infarction*

The paper on vectorcardiography has been written by an important investigator in this field. Doctor Wolff gives answers to perplexing questions for which the cardiologist and electrocardiographer have been waiting a long time.

It is true that at present the vectorcardiogram seems complicated and the machines are relatively expensive. In the illustrations the loops of the P-wave, the QRS complex, the terminal junction of the QRS, the RS-T segment and the T-wave all seem jumbled around the point of origin or O point. The vectorcardiogram must be photographed. However, improved equipment is on hand already and the vector curve is now larger and clearer, the components can be separated and prices will become more reasonable. The "initial," and the "early," the "main" or "overall," and the "terminal" portions of the QRS loop are more easily discerned as sharp entities in the illustrations. There is no doubt that these vector pictures will be still further magnified. Also, the junction or lack of junction of the end of the QRS with the T, that is, the ST segment, will be clearer, thus defining S-T elevations and depressions. A good start on all this has already been made in many laboratories.

Although the "vectorcardiographic" language and the illustrations may be difficult for the general medical reader, he will have gained a good deal if he senses the fundamental principles involved.

The internist and cardiologist are concerned with the future of vectorcardiography. Will it replace the electrocardiogram? Does the vectorcardiogram give a fundamental understanding of the electrical forces in the heart which the electrocardiogram fails to do, or is it good only for teaching, to explain the findings in the electrocardiogram?

There is another important question Do not the three basic leads, in planes at right angles to each other, called "A, B, C" by Grishman, and "X, Y, Z" by Wolff, give as much information as the vectorcardiogram, particularly, if they are taken simultaneously? May we not employ the VCG to learn more fundamental explanations of the ECG but nevertheless continue to use the ECG regularly, perhaps replacing the 12 leads that we now use by these three fundamental leads? Can we not improve our electrocardiographic interpretation?

This paper marks a landmark for it is the first time that the postmortem findings are correlated with the vectorcardiogram and the electrocardiogram in a considerable series of cases Doctor Wolff has found the *correlation of the VCG with the postmortem* far superior than in the case of the electrocardiogram His VCG diagnosis of *septal infarction* was confirmed again and again whereas it had been missed in the electrocardiogram

Doctor Wolff clearly points out the characteristics of the normal VCG in the three planes and the typical manner in which it is changed in ventricular hypertrophy and bundle branch block and by alterations in the position and rotation of the heart He then defines the VCG pattern in each type of infarction, distinguishing anterior, high posterior, inferoposterior and lateral wall infarctions, both by the orientation and direction of the abnormal vectors He shows how the relative positions of the end and the beginning of the vector loop distinguish acute infarction and acute pericarditis and how the shape of the T-wave differs in acute and healing or old infarction

#### *IV The Ventricular Pulsations in Myocardial Infarction, A Fluoroscopic and Kymographic Study*

For 15 years my colleagues and I have emphasized the ease with which abnormal pulsations of the left ventricle can be observed on fluoroscopy in patients with previous coronary occlusion We have often pointed out the diagnostic value of abnormal ventricular contractions However, we have not been successful in "selling" our ideas to the physician The average practitioner uses the fluoroscope to determine the size, shape and position of the heart but only the exceptional physician has become interested in the pulsations of the left ventricle as evidence of previous coronary occlusion Perhaps the trouble is that the doctor looks for a large ventricular pulsation whereas in reversal of pulsation at the apex, the movement is probably no more than 1/64th to 1/8th of an inch At first it requires concentration to see these movements The patient should take a very short breath and hold it without the slightest strain For timing, the out-thrust of aorta is considered systole With a little practice, it is easy to recognize reversal of pulsation due to previous infarction If there is difficulty, the doctor should move the screen away from the patient, toward himself, thus magnifying the border of the left ventricle Although he loses light intensity, the magnification more than compensates for this loss.



In addition to reversal of or paradoxical pulsation, the abnormalities to look for are localized diminution or absence of contraction. By "reversal" of pulsation is meant that the border of the left ventricle bulges out during systole, instead of moving in, this finding is almost pathognomonic of an infarct.

Some abnormality in pulsation is found in 75 per cent of cases of previous coronary occlusion. Reversal is found in half the patients. These abnormalities in left ventricular movement are not only of value diagnostically but also prognostically. As the patient improves, we have seen a definite "reversal" become an "absent" or "diminished" and finally a normal pulsation.

The abnormality in pulsation is located in the left lower one-third or one-half of the ventricle. Whether the infarction is diaphragmatic (inferior) or anterior, it is always seen in the usual posterior-anterior position or in a slight left oblique position. Occasionally, the left lateral also demonstrates the abnormality. Reversal of pulsation is found not only in ventricular aneurysm with a true eccentric bulge but also in the ordinary case of coronary occlusion in which the contour is smooth. It is the ordinary case to which reference is made by this reviewer.

We believe that, if the physician develops the habit of using fluoroscopy for this purpose, he will be more than rewarded in that he will have a good means of diagnosing infarction of the left ventricle secondary to coronary artery occlusion. In coronary insufficiency, on the other hand, the infarct is not through-and-through and a reversal of pulsation is not seen.

It has been suggested for many years that the diaphragmatic or inferior border of the left ventricle can be brought into the line of vision by distending the stomach with charged waters. This has proved of help to some.

An interesting future for fluoroscopy lies in improved screen. We have been told that there is a new screen in the making that will give many hundred times the light intensity of the present fluoroscopic screens. When this becomes a fact we will make tremendous advances in fluoroscopy of the heart.

# Pulmonary Function in Diseases of the Chest\*

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Pulmonary function tests are designed to provide accurate information of the extent and location of disturbed function thereby making available additional information for use with the history, physical, and roentgenological examination in the clinical management of the individual case. A battery of physiological test measurements are used, each possessing a wide range between the normal and the abnormal, and each covering an essential aspect in the evaluation of the adequacy of the gas exchange. One group of tests concerns the bellows action of the chest and lungs and evaluates the ability to move air in and out of the alveoli during the process of breathing. The other group of tests relate to the blood gas exchange across the alveolar-capillary or pulmonary membrane (oxygen and carbon dioxide transport). Pulmonary function measurements assist in the interpretation of the meaning of pulmonary disease from the standpoint of disability, operative risk and treatment.

The efficiency of the bellows action of the chest and lungs for moving air in and out of the alveoli is measured from spirogram tracings and from the residual capacity measurement.<sup>1</sup> Spirogram tracings provide measurements of total vital capacity, timed vital capacity, maximal breathing capacity, and a permanent graphic recording of the exhalation pattern. Evidence of air trapping in the lung is also obtained from the spirogram tracings by having the individual take a deep breath in and then blow out rapidly a few times. Total vital capacity is determined both in the supine and standing position, being the difference between the volume of the lung in the maximal distended position in inspiration and the minimal volume present at the end of a forced maximal exhalation. The total vital capacity in a normal individual is usually slightly larger in the standing than in the supine position. A marked reduction in total vital capacity in the standing position as compared to the supine position indicates the presence of severe pulmonary insufficiency. However, vital capacity when recorded with respect to time becomes a much more significant measurement. The subject is instructed to take in as deep a breath as possible, hold the breath momentarily and then on command blow all of the air out of the lungs as rapidly and as completely as possible. The volume exhaled in the first three seconds measured from the exact beginning of expiration is recorded as the three second timed vital capacity. The three second timed vital capacity is normally the same as the individual's predicted total vital capacity, and represents the maximal functional portion of the vital capacity (a respiratory rate of 15 per minute allows

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four seconds per breath, but if one second is utilized for inspiration only three seconds are left for expiration) The predicted total vital capacity is best computed from the height of the patient<sup>2</sup>

The maximal breathing capacity reveals the largest volume of air which an individual is able to move in and out of the lungs in a given short unit of time (12-15 seconds), but is expressed as liters per minute. The individual should be instructed to breathe as deeply and as rapidly as possible for 12 seconds, (never longer than 15 seconds), and the rate and depth varied on successive trials (not less than three) to get the maximal value. The 13½ liter respirometer\* was developed with the idea of providing an apparatus for mechanical recording with a minimal of breathing resistance for the deep fast breathing and to permit a quick accurate determination of the maximum breathing capacity value (5-10 minutes). The drum on the respirometer has a paper speed which provides a time interval of 12 seconds between the vertical lines. When the rate and depth of breathing are properly varied one can obtain precisely the highest maximal breathing capacity of which an individual is capable and the learning factor as such is not a significant feature. The maximal breathing capacity is a measure of the ability to use the lungs as a bellows and a very wide spread may exist between the normal and the most abnormal cases (10-200 liters per minute). The predicted\*\* maximal breathing capacity is based on the type of apparatus and procedure used and the age, sex, height and weight of the person<sup>1</sup>. If the maximal breathing capacity is normal, the individual is able to use the diaphragm well, the elasticity of the lungs is good, bronchospasm is not a factor and a significant degree of pulmonary emphysema does not exist. The degree of bronchospasm is measured quantitatively by comparing the maximum breathing capacity measurement before and immediately after one bronchodilator treatment using the intermittent positive pressure breathing method for administering a potent bronchodilator substance such as isuprel and vaponefrin<sup>3,4</sup>. The maximal breathing capacity and the timed vital capacity are independently variable measurements. It has been found in men that if the maximal breathing capacity is above 120 liters per minute, the degree of pulmonary emphysema present is insignificant and significant if less than 40 liters per minute, but between 40 and 120 liters per minute indeterminate<sup>5</sup>. The maximal breathing capacity is a sensitive test and this measurement frequently reveals early abnormalities and hence is valuable for screening purposes, either in the selection of problem cases requiring more complete pulmonary function evaluation or in the detection of poor risks in industrial workers exposed to irritating dusts<sup>6</sup>. The shape of the spirogram tracing as observed on the rapidly moving kymograph drum (32 mm in 12 seconds) reveals characteristic features of the expiratory flow. A slow and prolonged exhalation curve indicates obstruction to air flow, either of a fixed type or due to bronchospasm and

\*Made by Warren E. Collins, Boston, Mass

\*\*For the 13½ liter Collins respirometer the predicted maximal breathing capacity in liters per minute is men equal  $(97 - \text{Age}/2) \times \text{BSA}$  in Sq meters for women equal  $(83 - \text{Age}/2) \times \text{BSA}$  in Sq meters

the failure of the end exhalation point of the tracing to return at least to the beginning level indicates air trapping. If the spiogram tracings show a marked rise in the respiratory level during the maximal breathing capacity test with the rapid voluntary respiratory movements, this high inspiratory position indicates the presence of increased breathing resistance and usually the presence of a significant degree of pulmonary emphysema. Air trapping is a characteristic feature of asthma due to the bronchospasm as the bronchioles are narrower during expiration than inspiration, with a result that expiration is more difficult and prolonged.

The pulmonary function tests described thus far are easy to perform and the only special equipment required is the 13½ liter Collins Respirometer. These tests can be done in the office and on an average only five to 10 minutes are required to obtain satisfactory spiogram tracings. When the degree of bronchospasm is evaluated a slightly longer time period is required, since the bronchodilator should be administered over a period of at least 10 minutes to be certain of obtaining the maximal results.<sup>3, 4</sup> These tests are useful in evaluating the response to treatment, in following the clinical course of a disease by comparing serial spiogram tracings taken at intervals (similar to the chest roentgenogram) and in screening tests of candidates for surgery, anesthetic risk, workers exposed to lung irritants (either dust or gases) and other problem types of cases.

A second important basic measurement relating to the bellows action of the chest and lungs is the residual air capacity, which by definition is the volume of air remaining in the lung at the end of a maximal forced exhalation. The residual air occupies normally about 25 per cent of the total lung capacity, being slightly smaller in the younger age group (20 up to 35 years) and slightly larger in the older age group (30 over 60 years). In pulmonary emphysema the volume of residual air is increased in relation to the total lung volume and if this ratio is over 35 per cent a significant degree of pulmonary emphysema exists. The residual air is measured quantitatively using the oxygen open circuit method, and checked routinely on two runs to within 100 ml, if not the run is repeated. If the alveolar air contains more than 15 per cent nitrogen after breathing oxygen for seven minutes, impairment in the uniformity of air distribution in the lung exists.<sup>1</sup> The ratio of the residual air to the total lung capacity is most important in the individual case since this corrects for changes in total lung volume which may exist (either normal, increased or decreased). If the residual air occupies 35-45 per cent of total lung capacity a moderate degree of emphysema is present, from 45-55 of total lung capacity an advanced or severe degree and above 55 a far advanced or very severe degree of emphysema exists. The accurate diagnosis of pulmonary emphysema in some cases requires measurements of residual air, as the physical examination and the chest roentgenogram may be misleading or inconclusive. Pulmonary emphysema is frequently missed on the chest roentgenogram when a severe degree actually exists.

The three measurements of pulmonary function thus far described of greatest importance relating to the bellows action of the chest and lungs

and measuring independently variable aspects are (1) the timed vital capacity for three seconds, (2) the maximum breathing capacity and (3) the residual per cent of total lung capacity

A numerical ventilation factor (V F) has been used to evaluate the efficiency of the chest and lungs as a bellows from the average of the three measurements, all expressed as per cent of the normal predicted, namely: the three second vital capacity, the maximal breathing capacity and the residual air as per cent of total lung capacity. The ventilation factor provides a single figure value of the patient's ability to use the chest and lungs as a bellows for aerating the alveoli and this is well correlated with the arterial  $p\text{CO}_2$  in mm Hg as determined by direct tension measurements<sup>6</sup>

The second basic aspect of pulmonary function, namely the blood gas exchange across the alveoli-capillary membrane, is evaluated from studies of the arterial blood and the expired air. Normally, at sea level pressure, the arterial blood hemoglobin is 96-98 per cent saturated with oxygen both at rest and during exercise. The arterial blood oxygen saturation is obtained by dividing the corrected oxygen content by the corrected oxygen capacity as volumes per cent for each sample of blood. The Van Slyke manometric apparatus is used for the measurements of oxygen content and capacity. The double scale oximeter\* using the cuvette appears to be a fairly satisfactory procedure for determining the arterial blood oxygen saturation. A drop in the arterial blood oxygen saturation of 5 to 10 per cent or more below the resting level with exercise (after the one minute step-up test) indicates severe disability.<sup>1</sup> An increase in the exercise oxygen saturation above the resting level indicates less disability than implied by the resting level measurement.<sup>7</sup> It is thus of great importance to compare in each case where possible the rest and exercise arterial blood oxygen saturation, as often the exercise arterial blood oxygen saturation is of much greater value than the resting in evaluating the pulmonary function status. If the exercise arterial blood oxygen saturation drops 5 to 10 per cent below the resting level the individual should be restricted in such activities as walking up steps or up grades. In general, the exercise saturation tends to decrease in severe emphysema, but this is not always the case, and in pulmonary fibrosis without emphysema, a marked drop in the exercise arterial blood oxygen saturation frequently occurs.

An elevated arterial  $\text{CO}_2$  content indicates difficulty in blowing off  $\text{CO}_2$  and warns of the possibility of developing respiratory acidosis during infections or if the respiration be depressed by sedative drugs, anesthetics, or by other means. The arterial blood pH is the best single measurement revealing the exact status of the acid base balance concerning the presence of acidosis or alkalosis. If the patient has a marked degree of arterial blood oxygen unsaturation with an elevated  $\text{CO}_2$  content, then the administration of high oxygen concentrations with a mask or even with a catheter or tent may precipitate respiratory acidosis, drowsiness and even

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coma or death<sup>8</sup> In such a patient the sudden change to high oxygen breathing decreases the minute ventilation as a result of removing part of the stimulus to the respiratory center from the carotid bodies, as these are stimulated by the low oxygen in the blood and reflexively stimulate the respiratory center The high oxygen breathing relieves the arterial blood unsaturation and removes the stimulus from the carotid bodies and the ventilation decreases, in some to a critical level unless supplemented by mechanical aids

The expired air from the patient is studied with respect to the minute ventilation (total volume of air breathed during a test period of three to five minutes), the total oxygen uptake and the per cent of oxygen extracted from the inspired air breathed The minute ventilation is measured with respect to the number of liters per minute per square meter of body surface area If the minute ventilation is below the normal range, hypoventilation is indicated and if above hyperventilation In some cases hyperventilation may be the only abnormality revealed from the pulmonary function evaluation The one minute step-up exercise test (30 steps on an eight inch stool in one minute) has been standardized with respect to the normal range In some cases of marked pulmonary insufficiency the exercise minute ventilation may be inadequate in proportion to the step-up test requirement In general, the minute ventilation as a single measurement is often indeterminate as revealed from extensive statistical studies on a large series of cases The minute ventilation along with the data provided from the expired air gas analysis provides the necessary data to calculate the oxygen uptake The oxygen uptake is determined both at rest and with exercise The resting oxygen uptake tends to be in the normal range regardless of the degree of pulmonary insufficiency, and hence, is of little value in pulmonary disability evaluation On the other hand, the measurement of step-up exercise oxygen uptake is a very significant value A marked reduction in the exercise oxygen uptake in the presence of an adequate minute ventilation reflects the inability of the individual to expand the pulmonary bed and increase the pulmonary blood flow or to increase the cardiac output from the right heart to the elevated level representing a normal response proportionate to the degree of exercise given<sup>1</sup> If the normal amount of oxygen is removed from the expired air during the one minute step-up exercise an increased blood flow is necessary If the oxygen uptake is normal during exercise this indicates that the pulmonary blood flow is increased in proportion to the degree of exercise and that the pulmonary vascular resistance is not significantly altered A decreased oxygen uptake during step-up exercise indirectly indicates increased pulmonary vascular resistance, without the necessity of catheterizing the right heart to measure mean pulmonary arterial pressure and the cardiac output

The per cent of oxygen extracted from the inspired air breathed is a measure of the lung ventilation efficiency, and this figure is used to determine the oxygen uptake along with the pulmonary ventilation volume measurement Normally 4 to 5 per cent of the oxygen is extracted from

the inspired air at rest and 5 to 6 per cent during the step-up exercise. Thus, if a patient is removing only 25 per cent of the oxygen from the inspired air during exercise, twice the normal volume of air would be required for breathing to furnish the oxygen. In chronic pulmonary disease the per cent of oxygen extracted from the inspired air is usually decreased somewhat, but this measurement is usually indeterminate as to the degree of pulmonary function impairment present unless the decrease is of marked extent. Excitement with hyperventilation may result in a low abnormal value, which might be normal if the individual were breathing at a lower volume rate. A severe degree of pulmonary insufficiency may exist with hypoventilation present during step-up exercise and a normal per cent of oxygen extracted, but the total oxygen uptake would be decreased markedly.

The duration of dyspnea with a standard exercise test (such as the one minute step-up) is of value in pulmonary function evaluation. The one minute step-up test increases the oxygen uptake normally three to four times above the resting level and is designed as a test of pulmonary function rather than physical fitness. This test is satisfactory for routine use in studying patients with chronic pulmonary disease. The exercise study is of great value in demonstrating disturbances in ventilation-perfusion relationships (changes in the arterial blood oxygen saturation and total oxygen uptake). The duration of the dyspnea with the one minute step-up test is a subjective sensation on the part of the patient and it is subject to limitations as such, but careful observations by trained personnel minimize the subjective element. For the normal individual, the one minute step-up test is a mild exertion and the subjective dyspnea is less than 90 seconds in duration. A marked prolongation of the dyspnea constitutes a significant finding and indicates a severe degree of function impairment either cardiac or pulmonary. In general, the pulse and the respiratory rates are unreliable measurements on which to assess pulmonary function impairment. Statistical analysis of a large series of data on respiratory rate, pulse rate, and minute ventilation has revealed the inadequacy of these measurements alone as shown by the magnitude of the standard deviation.<sup>9</sup> Breath holding time has been found to be of no value. Tests of circulation times with ether and decholin, blood volume, hematocrit, hemoglobin level and venous pressure, and the electrocardiogram are frequently very helpful in differentiating the pulmonary and cardiac aspects of a given case.

Great advances have been made in research investigations relating to pulmonary function in recent years and many of these new tests are interesting and give promise of clinical value in the future, but as yet they are not sufficiently well established or the necessity proved to be routinely included in a pulmonary function evaluation. The direct tension measurements<sup>10</sup> of arterial  $pO_2$  and  $pCO_2$  is a valuable research procedure, but it is difficult to acquire a satisfactory proficiency in performance, hence subject to many errors by inadequately trained personnel. The use of the nitrogen meter<sup>11</sup> appears promising, but as yet the practicability and reli-

ability of both test and apparatus have not been adequately demonstrated. Pulmonary compliance,<sup>12</sup> relating to the pressure volume relationship of the lung, is a popular study at the present time, but whether this will provide any more practical clinical information over that which can be obtained with simple spirogram tracings remains to be demonstrated. Similarly the pneumotachograph is an interesting research instrument, but whether it provides any more information than can be obtained from the spirogram tracings on the respirometer remains to be demonstrated.

#### SUMMARY

An accurate evaluation of the degree of pulmonary function impairment may be made from the following physiological tests (1) Ventilation measurements from spirogram tracings (total vital capacity, three second timed vital capacity, maximal breathing capacity and the shape of the exhalation curve following a deep breath), (2) the degree of bronchospasm present, (3) the residual air capacity and alveolar nitrogen per cent after seven minutes oxygen breathing, (4) the arterial blood oxygen saturation at rest and immediately after step-up exercise, (5) the oxygen uptake during step-up exercise, (6) the per cent of oxygen extracted from the inspired air breathed and (7) the character and duration of dyspnea after step-up exercise.

#### RESUMEN

Una exacta valuación del grado de daño a la función pulmonar, puede lograrse mediante las siguientes pruebas funcionales (1) Medidas de ventilación por los trazos espirométricos (capacidad vital total, capacidad vital en tiempo de tres segundos, capacidad vital máxima y la forma de la curva de la exhalación después de una respiración profunda), (2) el grado de broncoespasmo presente, (3) la capacidad de aire residual y el nitrógeno alveolar por ciento después de siete minutos de respirar oxígeno, (4) la saturación de oxígeno de la sangre en reposo e inmediatamente del ejercicio del escalón, (5) la toma de oxígeno durante el ejercicio del escalón, (6) el porcentaje de oxígeno extraído del aire respirado y (7) el carácter y la duración de la disnea después del ejercicio del escalón.

#### RESUME

Les troubles de la fonction pulmonaire pouvant être évalués par les tests physiologiques suivants (1) mesure de la ventilation par tracés spirométriques (capacité vitale totale, capacité vitale mesurée pendant trois secondes, capacité ventilatoire maxima et aspect de la courbe expiratoire suivant une respiration profonde), (2) degré du bronchospasme existant, (3) capacité de l'air résiduel, et du pourcentage d'azote alvéolaire après sept minutes de respiration dans l'oxygène, (4) saturation oxygénée du sang artériel au repos, et immédiatement après des exercices de montée d'escalier, (5) augmentation de l'absorption d'oxygène au cours des exercices de montée d'escalier, (6) pourcentage d'oxygène retiré de l'air inspiré et (7) caractère et la durée de la dyspnée après exercice de montée d'escalier.



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# The Time Factor in Anesthesia\*

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Not more than 100 years ago, that is, before the discovery of anesthesia, time was the essence in doing surgery. Twenty minutes was the longest time any type of surgery could possibly be endured by a patient. After that time, the patient was likely to die from exhaustion or shock. "Have everything ready and do not lose time"—was the motto of the surgeon. Even 10 and eight years ago, it had great advantage for a patient to be operated by a surgeon who could work fast. At that time, only deep, third plane anesthesia could supply necessary relaxation, and we know that one-half hour of third plane anesthesia can mean shock for a patient who can easily endure four to five hours of light anesthesia. Ether, the anesthetic agent most commonly used to procure relaxation, has a considerable depressant effect on the myocardium in deep anesthesia, none in light anesthesia. The same is true for other agents. Moreover, during deep anesthesia, all the available anesthetic agents produce a profound depression of peripheral homeostatic mechanisms.

Recently, Rovenstine and his associates<sup>1</sup> demonstrated in dogs by direct microscopic observations of a portion of exteriorized omentum that, under light anesthesia by three different agents (cyclopropane, ether, sodium pentothal), the capillary circulation remained relatively unaffected, vasomotion of the metarterioles and precapillaries was preserved and venous return was rapid. The caliber of the small arterioles was normal with no appreciable dilatation, indicating good vasoconstriction. When a deep phase of anesthesia was reached, considerable impairment of the capillary circulation was seen while vasomotion was rapidly depressed and disappeared within one or two minutes. The response of the precapillary sphincters to epinephrine was depressed, circulation through the capillary bed was plethoric throughout, blood flow in the collecting venules was seriously slowed, and marked arteriolar dilatation was noted. Thus, the deteriorating effect of deep anesthesia was clearly demonstrated.

Fortunately, deep planes of anesthesia are not needed today. We can carry the patient in light anesthesia and supply the necessary relaxation by muscle-relaxant drugs. It could be shown in experimental and clinical work, and it is our own experience, that there is no deterioration of the homeostatic mechanism and no depression of the myocardium when muscle relaxants are used in adequate, non-excessive doses, if oxygenation and tidal exchange of the patient are taken care of adequately, and blood loss is replaced as it occurs.

Thus we can maintain a patient in good condition for any length of time in light anesthesia. Today there is no need for the surgeon to hasten

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He can be gentle and take whatever time is needed to perform his task, however delicate. There is no reason for the surgeon to rush except in order to stem unforeseen and excessive bleeding, and there should be no reason for the anesthesiologist to rush, except if something is wrong with the patient. Hypoxia should not be tolerated, obstruction should be diagnosed and taken care of immediately, deleterious positions should be corrected at once. On the other hand, the qualifications of an anesthesiologist should not be judged by how fast he is ready for the surgeon.

The statement has been made not long ago that the great success in a series of heart operations was mainly due to fast intubation. Even more amazing is the fact that a group of good anesthesiologists preface their original article with the following statement<sup>2</sup>

"The adoption of the routine use of detergents for the surgical scrub has deprived the anesthesiologist of the minimal 10 minute period for induction and intubation which was previously available to him. At present the interval of time which elapses from the time the surgeon sees his patient immediately preoperatively, until he is ready to begin the operation averages five minutes."

Thus these anesthesiologists draw the conclusion that these five minutes have to suffice for them to get the patient ready for the operation. Fifteen to 20 minutes may be necessary to put the patient in the correct position (say in chest surgery), the operation may last four to five hours, but five minutes is all the anesthesiologist gets to be ready. For this reason, these authors recommend their method of fast intubation. They use rapid injection of a predetermined amount of an ultra-short acting barbiturate combined with a curare preparation, a standard mixture of 400 mgr thiopentothal (8 cc of a 5 per cent solution) and 4 mg of deca-methonium bromide. The 5 per cent solution of sodium pentothal instead of the usual 2½ per cent is chosen to increase the rapidity of the injection, the entire injection thus requiring five seconds. After 20 to 25 seconds the patient can be intubated. The time required for induction and intubation using this technique was not permitted to exceed 60 seconds. Many similar procedures are being recommended.

One may question whether the fact that the surgeon is ready after five minutes of scrubbing is a reason to hasten induction and intubation to such a degree, and whether there are any advantages to the procedure. How does this method compare with the more conservative procedures, where induction is accomplished by intermittent injection of an ultra-short acting barbiturate watching the patient's blood pressure closely, and stopping when the lidreflex disappears, keeping the patient breathing and well oxygenated for several minutes while supplying small amounts of ether or gas, and eventually injecting the selected type of curare before intubation, taking five to 10 minutes, instead of 25 seconds.

In a paper evaluating a new ultra-short acting barbiturate (surital sodium) Phillips<sup>3</sup> states that, immediately following the injection of the drug, a drop in blood pressure is noted proportional to the rapidity of the injection and to the larger initial dose. Stephen et al,<sup>4</sup> in an article on

"Hypotension under Anesthesia" state that rapid injection of ultra-short acting drugs into the bloodstream may produce specific effects in the cardiovascular system of man, including a drop of blood pressure and a reduction of cardiac output due to direct depression of the myocardium. A considerable fall of blood pressure was noted by the writer<sup>5</sup> after rapid intravenous injection of sodium secenal, this is not present when the drug is injected slowly.

In order to clarify the problem, the Duke group of Anesthesiologists<sup>6</sup> set up an excellent investigation. Two hundred and thirty-eight patients were given the "shot gun" method under carefully controlled conditions. Twenty-two had the conventional slower induction. ECG, blood pressure, and pulse rates were recorded preoperatively, after injection of the muscle relaxant, and again after injection of the barbiturate. There was a persistent fall in blood pressure, whether sodium pentothal, sodium surital, or evipal was administered rapidly, a decrease of 40 mm Hg or more of the systolic pressure took place in about 1/3 of the patients. In five patients, blood pressure could not be obtained in the interval between administration of the hypnotic and laryngoscopy. One good-risk patient developed cardiac arrest two minutes after the barbiturate was injected, and in two patients of this series, operation had to be cancelled due to persistent hypotension. It is interesting that a 40 to 50 mm fall in blood pressure was also noted in the series of the group that advise the "shot gun" method of intubation in order to save time.

On the other hand, not one of the 22 patients observed by the Duke group using the intermittent administration of sodium pentothal, followed by the intravenous use of a muscle relaxant and nitrous oxide inhalation, had a fall in blood pressure of more than 20 mm Hg, a fact which confirms our observations. There were no significant changes in the ECGs of these 28 patients.

In both series of patients investigated during rapid injection of the barbiturates, the blood pressure fall was rectified, with only four exceptions, during intubation. The blood pressure rapidly rose to preanesthetic levels, together with an increase in pulse rate, probably due to sympathetic impulses caused by laryngoscopy and intubation. The latter were accompanied by arrhythmias. It is well known that direct laryngoscopy and tracheal intubation uncomplicated by coughing, anoxia or hypercapnia, may produce considerable rise in blood pressure and an increase in heart rate. Driggs and his co-workers<sup>7</sup> state that this rise in blood pressure and the cardiac acceleration represent a stress placed upon the myocardium. They could record rises in systolic pressure of more than 90 mm Hg during intubation under light anesthesia, and therefore advise intubation in second or third plane anesthesia.

The considerable fall in blood pressure followed by such a considerable rise may often escape the attention of the anesthesiologist using the rapid intubation method. After all, only one or two minutes are involved, he is very busy, and when he takes the blood pressure after intubation, the preanesthetic level has been reached, and the patient seems in good condi-

tion. Two wrongs seem to make one right, and apparently in most cases one can get by with it. This is certainly not true in all cases obviously not in a patient with a severe mitral stenosis, who has a relatively fixed cardiac output; or in a patient with advanced aortic stenosis where adequate circulatory compensation cannot be maintained after such rapid changes. Likewise, a heart damaged by previous myocardial infarction poorly tolerates rapid alterations of circulatory dynamics.<sup>2</sup> Even in a normal heart the rapid alterations in cardiac function following rapid injection of a potent ultra-short acting barbiturate cannot be ignored. Moreover, it cannot be predicted which patients would react with the greatest fall of blood pressure, and which would have more numerous irregularities.<sup>6</sup> There seems to be no direct correlation as to age or general status of the patient. Besides, and most astonishing, no relationship can be demonstrated between the appearance or not of the undesired effects, and a smooth intubation or a difficult one with bucking or coughing on the tube or even laryngospasm.

For these reasons, it is more desirable to administer the ultra-short acting barbiturate intermittently over a longer period of time, and to attempt laryngoscopy and intubation in a slightly deeper plane of anesthesia, by introducing potent analgesic drugs like ether or cyclopropane for a short time. Thus, it is desirable to take a few more minutes to get ready for the surgeon. The safety of the patient should be the first consideration of the surgeon *and* of the anesthesiologist. As the time factor fortunately no longer plays an important role in considering the allotted time for a surgical procedure, it should not be given any importance in itself in getting the patient ready for surgery.

#### SUMMARY

Light anesthesia with the common anesthetic agents does not significantly interfere with the homeostatic mechanisms, nor does it depress the myocardium. The same is true for adequate amounts of muscle relaxant agents. Problems of respiratory physiology and blood replacement are well understood. Thus, practically limitless operating time can be afforded the surgeon. Therefore, no undue pressure should be exerted on the anesthesiologist limiting the time allotted for induction and intubation.

Various dangers inherent in the method of rapid intubation are pointed out and discussed.

Intermittent intravenous injection of the barbiturate and addition of small amounts of potent inhalant anesthetic agents for intubation in a slightly deeper plane of anesthesia are recommended. This would avoid those rapid changes of circulatory dynamics which are encountered when using the "gun shot" method of induction and intubation.

#### RESUMEN

La anestesia ligera con los agentes comunes, no interfiere de modo importante con los mecanismos homeostáticos ni deprimen el miocardio. Lo mismo ocurre con respecto de los agentes relajantes del músculo a dosis

adecuadas Así, prácticamente el cirujano dispone de tiempo ilimitados Por tanto, no debe hacerse presión sobre el anestesista limitado el tiempo concedido para la inducción y la intubación

Se señalan varios peligros inherentes al método de la intubación rápida y se discuten

La inyección intravenosa de barbitúricos y el agregado de pequeñas cantidades de agentes anestésicos potentes por inhalación para la intubación en un plano ligeramente más profundo de anestesia, se recomiendan Esto evitaría los rápidos cambios de la dinámica circulatoria que se encuentran al suar al método repentino de inducción e intubación

### RESUME

Une anesthésie légère avec les produits habituels n'a pas d'action importante sur le mécanisme circulatoire et ne cause pas de troubles myocardiques Les mêmes constatations s'appliquent lorsqu'on utilise à dose correcte l'action des agents susceptibles de créer la relaxation musculaire Les problèmes de la physiologie respiratoire, et de la transfusion de remplacement sont bien établis Ainsi le chirurgien peut se permettre d'opérer pendant un intervalle de temps pratiquement illimité C'est pourquoi on ne devrait pas insister auprès de l'anesthésiste pour limiter le temps nécessaire à la mise en train de l'anesthésie et à l'intubation

L'auteur met en évidence les différents dangers qui peuvent survenir lorsque l'intubation est faite rapidement, et il en discute la signification

L'auteur préconise des injections intra-veineuses intermittentes de barbiturique et l'addition de petites quantités d'agents anesthésiques par inhalation pour l'intubation de façon à réaliser un plan d'anesthésie très progressivement croissant Ainsi seraient évitées les modifications rapides de la dynamique circulaire qui surviennent lorsqu'on pratique une méthode de mise en train de l'anesthésie et d'intubation brutale, en "boulet de canon"

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# Palliative Procedures for the Treatment of Carcinoma of the Esophagus\*

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Not too many years ago, it was predicted that the esophagus would never yield to surgical attack. Development of improved technics in thoracic surgery and related specialties has made possible the resection of the esophagus with decreasing rates of mortality and morbidity. A state of optimism then arose in association with treatment of cancer of the esophagus. Surgeons have been developing more extensive procedures for managing the more advanced forms of cancer. Longer lengths of the esophagus can be resected successfully now. The structures within the mediastinum are involved by carcinoma early, although the esophagus may be resected, the related structures cannot be.

Surgical technics now make possible the resection of any portion of the esophagus and the re-establishment of continuity at any level in the thorax or cervical region by anastomosing either the mobilized stomach, jejunum, or colon to the proximal esophageal segment. The reconstructed esophagus may be placed in either the old esophageal bed, the right or left pleural cavity, the anterior mediastinum, or in the subcutaneous tissue of the chest.

Results in the treatment of carcinoma of the esophagus by surgery and by other means have been discouraging. However, there have been enough cures or long-term survivals to give hope to the patient and doctor. When the esophageal growth appears resectable and the patient's physical condition adequate, the patient should be offered surgical therapy. This does not mean though that the surgeon is to make an heroic effort to resect a non-resectable lesion or to do a more extensive procedure than the physical status of the patient can tolerate or the end result can justify.

In a few patients at the time of the clinical work-up, and in many patients at the time of exploration, it is discovered that the lesion in its entirety cannot be resected. For this clinical group many surgeons yet will advocate resective surgery with removal of as much of the tumor as possible. For a large percentage of these cases, there are indications that the same results can be obtained with procedures of lesser surgical magnitude. Also, there are many patients who, because of unrelated diseases in other organs, are unable to tolerate major degrees of surgical trauma.

In any case, the surgeon is confronted with the responsibility of re-establishing or maintaining the oral intake of food and water. There are today palliative technics of varying degrees of surgical magnitude.

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for restoring or preserving the patency of the esophagus. There is little excuse for refusing a patient one of these latter procedures which have a comparatively low incidence of mortality and morbidity.

These procedures can be used as a final therapeutic agent or as a preliminary stage of a more radical approach.

### 1 *Gastrostomy or Jejunostomy*

Used as a palliative measure in a patient with a non-resectable esophageal lesion, gastrostomy or jejunostomy prevents starvation only. There is a relatively high postoperative mortality associated with these procedures. Obstruction is not relieved, the source of pain is not removed, nor is prevented the accumulation of the troublesome pharyngoesophageal secretions which continue to be aspirated into the tracheobronchial tree, preventing comfort or sleep. Gastrostomy feedings have a demoralizing effect upon the patient. There is an indication for a gastrostomy or jejunostomy only in the patient who cannot tolerate a more extensive surgical procedure and at the same time has such a severe curvature of the spine that endoscopy cannot be carried out.

As a pre-resective measure, gastrostomy or jejunostomy cannot be considered effective procedures for getting a patient in better nutritional status.

In conjunction with retrograde dilatations with Tucker bougies during and following deep therapy, there may be an indication for a Spivack gastrostomy. In post-irradiation patients, it is possible that the lumen could be maintained by this method in a large percentage of the cases of the more stenosing, fibrous lesions.

### II *Endoscopy and Dilatations*

Esophagoscopy and gentle, careful dilation of the obstructed lesions with one of the various types of dilators can produce immediate relief. This procedure has less associated risk than a resection, particularly a high resection in an emaciated, dehydrated patient. Vinson reports a perforation rate of only 1 per cent.

It seems unfortunate that many thoracic surgeons, for various reasons, themselves do not perform esophagoscopies or dilate carcinomatous lesions. It would seem that the same surgeon, at the time of esophagoscopy or at the time of thoracotomy, weighing the indications for the procedures and the risks of mortality, would rather accurately evaluate the situation into which he would be placing himself.

Dilatations should be used more often for the purpose of getting a patient with an obstruction in good physical condition for surgery. If a repeat esophagoscopy is necessary, a catheter may be passed into the stomach for feeding purposes. Gastrostomies can be avoided except in rare cases.

There is an indication for dilatation also in those patients who are considered candidates for irradiation therapy. Adequate roentgen therapy in poor risk patients has an associated high mortality. The use of a catheter for a few days following dilatation will prevent re-obstruction.



by the tumor or by temporary congestion and edema which could be expected to take place at the site of irradiation. In the case of partial obstruction, a thread can be left in the lumen at the time of dilatation to act as a guide for subsequent dilatations should deep therapy produce post-irradiation swelling.

Esophagoscopy with dilatation often can maintain an opening in a post-irradiation case. I have used the Huist mercury bougie for this in some cases, and, in others, the esophagoscope with Jackson dilators. The method of anchoring a silk thread in the intestine and passing threaded dilators along this guide has been used by Vinson. Dilatation therapy for lesions immediately adjacent to the left bronchus or the aortic arch should not be used, because of the possibility of producing bronchial or aortic fistula. Palmer cautions against using a larger dilator than the number 18 French bougie, while Vinson has used a number 40 French bougie.

### III *Intubation*

Carter Symonds was the first to intubate the esophagus, using a gum-elastic tube. In 1927, Souttar reported an improved tube for this purpose which consists of a close spiral of German silver wire. The proximal end of this tube has a collar which tends to prevent its onward passage. Its flexibility enables it to conform to the lumen of the esophagus. Allison and Bonnie, who re-evaluated this method in 1949, considered the Souttar tube still of usefulness in selected cases. In 1949, Brown reported on the use of a silver tube which he had inserted orally into the esophagus. Ravitch has reported a case in which, following an exploration of a non-resectable lesion, a plastic tube was inserted orally through the stricture before the chest was closed. In selected cases intubation can afford many months of relief for the patient before distant metastasis or complications prove fatal.

### IV *Local Excision of the Obstructive Growth and Bridging of the Defect with a Prosthesis*

In 1922, Neuhof and Ziegler performed in experimental animals a two-stage procedure which consisted, in the first step, of packing off a local area of the esophagus to produce a granulation tissue barrier. At a second stage, the esophagus was resected and the defect bridged with a rubber tube. Berman, since that time, has modified this work by performing a local excision of the esophagus and immediately bridging the defect by using a flanged, flexible polyethylene tube. This technic has been used in a small group of patients with favorable results.

It would seem that indications for this procedure could be found in the following instances: at the time of exploration, when the lesion is found to be non-resectable, in the case of the patient with low surgical reserve, and, during surgery, should situations arise that make it unlikely that the patient can withstand a continuation of extensive resection.

### V *Shunting Techniques*

Non-resectable lesions of the lower esophagus can be by-passed readily by severing the esophagus above the lesion and carefully closing the distal

end The proximal end can then be anastomosed, less often to a loop of the jejunum, and more often to a Roux-Y segment, which can be brought up through the diaphragm and lateral to the esophageal opening Non-resectable lesions at higher levels can be treated similarly by primary anastomosis with a longer Roux-Y segment An alternative is Yudin's technic of bringing the jejunum through a subcutaneous tunnel to the cervical esophagus and performing the anastomosis at a second stage

## VI *Irradiation Therapy*

Irradiation therapy can be given by radium bougie, direct implantation of radioactive material, or deep irradiation using various voltages and technics Discouraging surgical results, particularly in the experience with the high thoracic and cervical lesions, are forcing a re-evaluation of irradiation therapy There are two facts concerning irradiation that are worth remembering 1) Following therapy many patients rapidly recover ability to swallow This recovery often remains for the duration of the illness, although death occurs from extension of the tumor 2) Following therapy death frequently occurs from perforation of the esophagus either into the mediastinum, pleural cavity or aorta Autopsy in such cases has revealed no evidence of residual carcinoma These facts suggest certain therapeutic possibilities

Used as a preoperative measure, short periods of deep therapy will relieve obstruction and clear up much of the sloughing, ulcerating and infected tumor Having had a period in which there could be normal oral intake of food and fluids, a patient could come to surgery in good nutritional and mental balance I have had two patients who received preoperative irradiation therapy Both underwent palliative intrathoracic esophagogastrostomy There is no question that their preoperative condition was greatly improved by irradiation, and I do not believe that the dissection was more difficult because of it

The idea of resection and postoperative deep therapy has been suggested by others, and a controlled series should be evaluated

As a curative or palliative method, several technics for administering irradiation have been suggested

In Denmark, where little esophageal surgery is done, Neilson advocates the technic by which the patient is placed on a special stool and rotated with the esophagus as the axis of rotation Rotation takes place at right angles to the field of irradiation, in order that the maximum dosage is delivered to the tumor with a minimal dosage to the skin Twenty-five per cent of his cases were alive at the end of one year, and 15 per cent, at the end of two years Sweet's surgical series, which may be more selective, reveals 42 per cent alive at one year, and 34 per cent, at two years

In this country the multiple-port method for irradiating esophageal lesions has produced comparative results

Negus has used a local irradiation technic Using the esophagoscope, he gently dilates the lesion with a bougie and measures the exact length of the tumor mass Radium or radon seeds are secured at one-centimeter intervals along a small rubber or plastic tube that projects one centimeter

beyond either end of the growth. Three to four of these tubes are inserted and left for a period of approximately 10 days. It would be interesting to see a series of cases treated by this method in conjunction with external irradiation.

#### SUMMARY

The importance of careful selection of the therapeutic plan for a given case of esophageal carcinoma is emphasized. There must be on the part of the physician and surgeon a willingness and ability to modify a given plan should unfavorable situations exist or arise. There will continue to be many cases in which major curative or palliative resections cannot be done, either because of the general physical condition of the patient or because of the non-resectability of the esophageal growth. In these cases, other procedures of lesser magnitude than a resection can and should be used.

Longer survival and more comfort to a greater number of patients can result from making proper choices of the curative and palliative techniques now available for treatment of carcinoma of the esophagus. The patient who is discharged from the hospital with a gastrostomy, who either has been refused esophageal therapy or has been given an exploratory operation without having deglutition re-established, has not been afforded the best medical care.

#### RESUMEN

Se recalca a importancia de una selección del plan terapéutico en un caso dado de carcinoma del esófago. Debe haber por parte del cirujano y del médico una buena voluntad y disposición para modificar un plan cuando existen desfavorables situaciones o estas aparecen. Habrá continuamente muchos casos en los que las resecciones mayores curativas o paliativas, no puedan hacerse ya sea por mal estado general, o por imposibilidad quirúrgica.

En estos casos deben usarse otros procedimientos de menos magnitud que la resección deben llevarse a cabo.

Se obtendrá una más larga sobrevivencia y comodidad para mayor número de enfermos como resultado de la selección adecuada de las técnicas curativas y paliativas ahora asequibles para el tratamiento del carcinoma del esófago. El enfermo que es dado de alta con una gastrostomía ya sea porque haya rehusado la terapia del esófago o bien porque se haya hecho una exploración sin restablecimiento de la deglución, no ha obtenido del mejor cuidado médico.

#### RESUME

L'auteur insiste sur l'importance d'une mise au point prudente du plan thérapeutique dans un cas déterminé de cancer oesophagien. Il doit exister de la part du médecin et du chirurgien la bonne volonté et la possibilité de modifier le plan déterminé dès que l'on constate ou qu'il se produit des faits qui semblent défavorables. On doit compter encore avec un nombre important de cas pour lesquels la résection majeure, soit curative, soit palliative, ne peut avoir lieu. Elle sera empêchée ou bien par l'état gén-

éral du sujet, ou à cause de l'impossibilité de sectionner la tumeur oesophagienne Dans ce cas, des procédés qui n'ont pas l'importance de la résection peuvent et doivent être utilisés

Un choix meilleur des possibilités techniques actuelles pour le traitement curatif ou palliatif du cancer de l'oesophage peut permettre une plus longue survie et des conditions plus faciles à supporter pour un assez grand nombre de malades Le malade qui quitte l'hôpital avec une gastrostomie soit que le traitement oesophagien n'ait pu être réalisé, ou bien que l'intervention exploratrice n'ait pas permis le rétablissement de la déglutition, n'a pas bénéficié du maximum des possibilités médicales

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# Fluoroscopy of the Chest

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A postero-anterior teleoroentgenogram of the chest is primarily a "scout" film, and diagnosis based solely on such an examination is often little more than guesswork. However, this film serves admirably in *detecting* most lesions, and aids in determining what additional studies need to be performed. Unless the clinical or roentgen diagnosis is evident, one should then proceed with further roentgen study.

As a general rule this should begin with fluoroscopy. A complete chest fluoroscopy can be accomplished within a few minutes if the examiner applies a well-organized approach. For purposes of instructing students and residents, we have divided pulmonary fluoroscopy into five phases which we have designated as *Observation, Rotation, Breathing, Ingestion* and *Tilting*. Their first letters spell the word *ORBIT*, which serves as a mnemonic.

1 *Observation* After preliminary fluoroscopy of the entire chest, including the heart, attention is directed to the lesion in question. Its size, shape, homogeneity and margination are closely studied. The presence or absence of pulsation should be noted. However, this is of little significance unless opposite sides of the lesion can be seen simultaneously, since differentiation between transmitted and intrinsic pulsation cannot otherwise be made. Even under those conditions aneurysms cannot be reliably distinguished from tumors, since aneurysms often contain clot which interferes with expansile pulsation, and tumors occasionally surround a vessel and may then appear to pulsate expansively.

2 *Rotation* By slightly rotating the patient (10 to 20 degrees) one can quickly establish whether a density lies anteriorly or posteriorly. Storch<sup>1</sup> utilizes the sternum and spine as reference points. If, on rotation, the lesion moves in the same direction the spine moves, it is posterior, whereas if it moves with the sternum it is anterior in location (Fig 1). The amount of movement of the lesion indicates how far it lies from the center of the thorax (the vertical axis on which the patient is rotated). Thus, peripheral lesions shift more with rotation than central ones.

Rotation serves to separate a lesion from adjacent structures so that a clearer view of it is obtained. Obviously, if the lesion can be separated entirely from a superimposed structure by rotation, there is little likelihood that it is connected with that structure. Rotation is also helpful in differentiating hilar node enlargement from vascular shadows, the nodes remaining rounded while vascular shadows elongate or disappear as the patient is turned.

As a lesion comes closer to the fluoroscopic screen, its image appears smaller and sharper. If a density is smaller in the postero-anterior projec-

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FIGURE 1A

FIGURE 1B

FIGURE 1C

*Figure 1* Right superior mediastinal mass localized by rotation during fluoroscopy Spot films *A* Straight frontal view *B* Ten degrees rotation to right *C* Twenty degrees rotation With increasing rotation, the lateral border of the mass (retouched) shifts away from the right border of the spine (dotted line) and moves in the same direction as the manubrium (retouched), but to a slightly less degree This indicates that the mass lies far anteriorly in the thorax A thymic cyst was found at operation

tion (patient facing the screen) than in the antero-posterior, it lies in the anterior half of the thorax. The patient must be in true frontal position and in contact with both table top and screen for the results of this maneuver to be valid.

Another method of localization can be utilized. With the patient facing the screen, the shutters are opened fairly wide and the screen positioned so that the image of the lesion lies on one side of the visible fluoroscopic beam. The screen is slowly shifted transversely in the direction of the lesion, which now seems to move. The greater this apparent movement, the more posterior is the lesion. Localization by this method requires considerable practice and experience, so it is not widely used. However, by taping a coin to the skin over the image of the lesion and observing the relative movement between the coin and the lesion as the screen is shifted, the interpretation is simplified.

3 *Breathing* It is important to study the movement of the abnormal shadow as the patient breathes. During inspiration the spine remains relatively immobile while the ribs move upward, the diaphragms and lungs move downward, and the vascular markings spread apart. By careful observation during respiration it is often possible to relate a lesion to the mediastinum, thoracic wall, heart, diaphragm, or lung. A point of reference is taken in sequence on each structure in close proximity to the abnormal density, and the relative movement between this structure (rib, vertebra, segment of the heart, etc.) and the density in question is noted. If the two move together as a unit, a connection between them is postulated, but even the slightest amount of independent movement indicates that they are not intimately associated.

A recent case serves to illustrate the value of this technic (Fig 2). A mass was discovered in the left lower posterior thorax adjacent to the

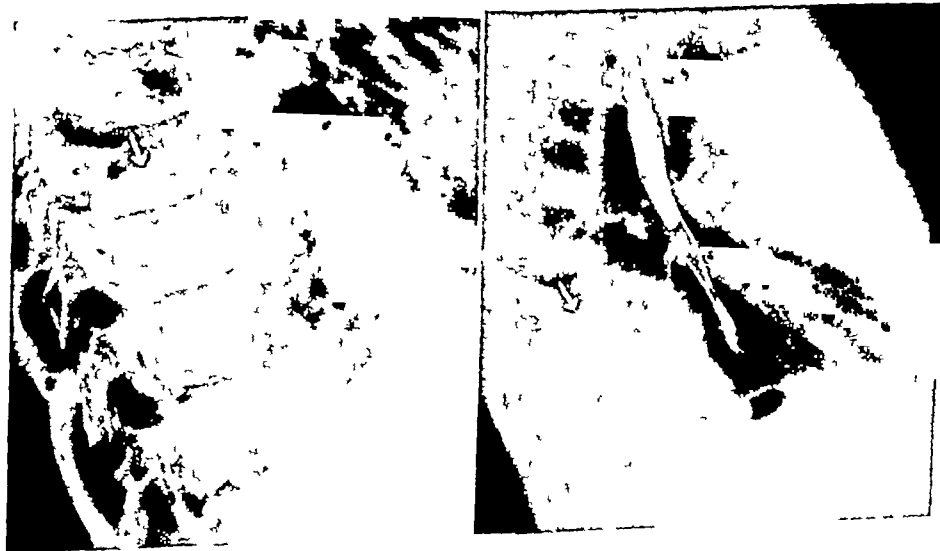


FIGURE 2A

FIGURE 2B

*Figure 2* Mass in posterior segment of left lower lobe. Upper border of the mass (arrow) moves slightly in relation to the overlying ninth thoracic vertebra and posterior ribs (see text). The localization was confirmed at operation. A Inspiration  
B Expiration

spine Fluoroscopically, the left diaphragm showed limitation of motion With respiration the mass moved slightly in relation to the adjacent immobile vertebral bodies and the superimposed posterior ribs It was, therefore, concluded that the mass did not arise in the spine or chest wall, but was primarily a lower lobe lesion This was also supported by the observation that the mass moved as a unit with the vascular markings in the adjacent lung At operation, the mass was found in the posterior basal segment of the left lower lobe

The effect of respiration on the heart and mediastinum should also be carefully observed In obstructive emphysema, as well as in collapse, the mediastinal structures shift in the direction of the lesion on inspiration and in the opposite direction on expiration The paradox of enlargement



FIGURE 3A

FIGURE 3B

*Figure 3* Paradoxical respiratory effect on heart during an attack of bronchial asthma Fluoroscopy revealed limited diaphragmatic excursions with minimal increase in heart size during expiration A Inspiration B Expiration



FIGURE 4A

FIGURE 4B

*Figure 4A* Teleoroentgenogram in a cardiac patient with unexplained chronic pulmonary infiltrate at the right base—*Figure 4B* Esophago-gastric junction filled with barium, revealing an unsuspected cardiospasm The lung changes were attributable to aspiration of esophageal contents



of the heart shadow on inspiration and shrinkage on expiration occurs in bilateral obstructive emphysema, as seen in bronchial asthma, the "bronchiolitis" of infants, and in partial tracheal obstruction<sup>2</sup> (Fig 3)

The Valsalva and Muller maneuvers,<sup>3</sup> coughing, sniffing, and snorting may aid in differentiating between a vascular shadow and a non-vascular mass, since alteration of the intra-alveolar pressure causes vascular structures to change in size. These techniques may profitably be combined with trendelenburg and upright positions in the study of mediastinal masses.<sup>4</sup> They are of particular help in differentiating mediastinal lymph node enlargement from vascular shadows. Diaphragmatic excursion can often be accentuated by sniffing.

4 *Ingestion* Ingestion of barium is an integral part of chest fluoroscopy and should never be omitted. By this means an unsuspected esophageal abnormality which is the underlying cause of the pulmonary disease may be shown (Fig 4), or gastro-intestinal segments in the thoracic cavity, directly accounting for the abnormal roentgen appearance, may be revealed.

Evidence of impingement on the esophagus often aids in the localization of a mass lesion and may be the only indication of enlarged mediastinal lymph nodes. This is especially true of the bifurcation nodes, enlargement of which often produces an extrinsic pressure defect on the esophagus at the level of the carina, usually best seen in the left oblique view (Fig 5). This may be the only clue to a correct pre-operative diagnosis of pulmonary carcinoma, as pointed out by Fleischner.<sup>5</sup>

5 *Tilting* Examination of the patient in the prone, supine, trendelenburg, lordotic, or decubitus positions is often rewarding. The decubitus examination may be made by utilizing a stretcher in front of the upright fluoroscope, but tilting the upright patient to right and left in the frontal view, and bending at the waist in the lateral view are more practical methods. The lordotic position<sup>6</sup> is easily assumed during upright fluoroscopy, and is accomplished through the use of sand bags under the lower

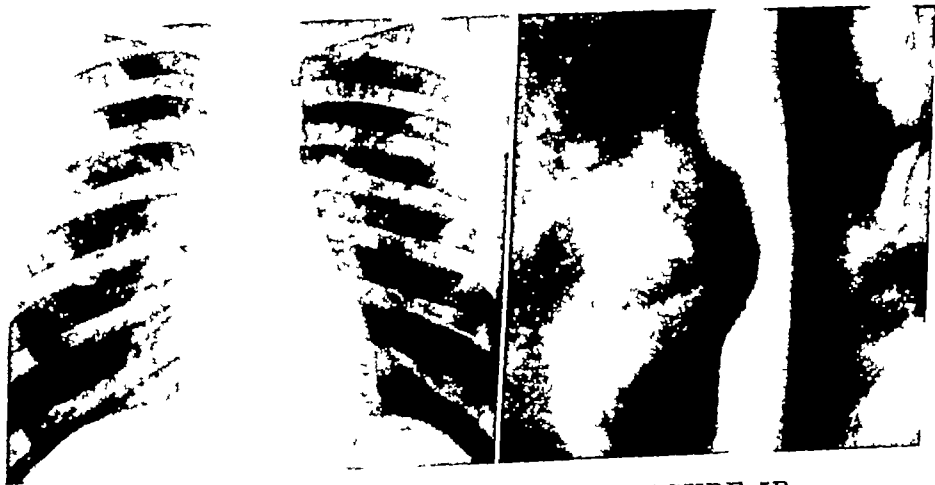


FIGURE 5A

FIGURE 5B

Figure 5A Teleoroentgenogram of chest. The right hilum is enlarged and is more dense than the left—Figure 5B Left anterior oblique view of the middle third of esophagus showing the indentation caused by enlarged carinal lymph nodes

ribs in supine fluoroscopy The recognition of pleural fluid, the demonstration of fluid levels, the delineation of middle lobe disease, and the displacement of pulmonary densities from overlying structures are facilitated by applying these gravitational methods

### *Roentgenography*

The exposure of spot films during fluoroscopy is an important part of the examination since it provides a permanent record of the findings, and brings out details that are difficult to demonstrate by other means<sup>7</sup>

After fluoroscopy, additional films are obtained as indicated The proper degree of rotation for oblique projections and the need for such positions as the lateral, lordotic, decubitus, supine, prone, and erect are determined at fluoroscopy Expiration films are obtained when indicated by fluoroscopy, and centering for detail roentgenograms and laminagrams<sup>8</sup> is also facilitated

In addition to fluoroscopy, many other roentgen methods of examination of the chest are available Excellent descriptions of these can be found in articles by Cohen and Geffen,<sup>9</sup> Rigler,<sup>10</sup> and Robbins, Hale, and Merrill,<sup>11</sup> and only brief mention of them is made here Bucky films of the chest, spine, and upper abdomen, stereoscopy, laminagraphy in frontal, lateral, and oblique planes, selective and "lung mapping" bronchography, pulmonary angiography, and diagnostic pneumothorax and pneumoperitoneum all have their specific indications

However, there is no adequate substitute for careful chest fluoroscopy As one gains experience with this oft-neglected method, the realization of its value in the problem case is soon appreciated

### SUMMARY

The chest teleoroentgenogram serves as a "scout" film for the detection of intrathoracic lesions When the diagnosis is not apparent, further roentgen study of the patient is indicated, and, as a rule, this should begin with fluoroscopy

Adequate fluoroscopic examination of a chest lesion should include the following

- 1 Observation of the finer details of the lesion
- 2 Rotation of the patient to determine relationships between the lesion and the adjacent normal structures
- 3 Breathing maneuvers to detect vascular components and to assist in localization
- 4 Ingestion of barium to ascertain origin in, or displacement of, the gastro-intestinal tract
- 5 Tilting of the patient into various positions to evaluate the effects of gravity on the lesion

Exposure of spot films during the fluoroscopic examination is essential to provide a permanent record of the findings, and additional views should

be obtained after fluoroscopy to bring out further details

Fluoroscopy is one of the most important and rewarding methods of roentgen examination of the chest

### RESUMEN

El roentgenograma del tórax, sirve como una película de "exploración" para el descubrimiento de las lesiones intratorácicas. Cuando el diagnóstico no es aparente, se requiere un estudio ulterior y como regla éste debe empezar por la fluoroscopia.

El examen fluoroscópico adecuado debe incluir lo siguiente:

- 1 Observación de los más finos detalles de la lesión
- 2 Rotación del enfermo para determinar las relaciones entre las lesiones y las estructuras próximas
- 3 Provocación de la respiración para descubrir la participación vascular y ayudar a la localización
- 4 Ingestión de bario para aclarar el origen en o el desplazamiento del tubo digestivo
5. Movilizar el enfermo en formas varias para estimar el efecto de la pesantez sobre las lesiones

La toma de películas enfocadas, durante el examen fluoroscópico es esencial para obtener un registro permanente de los hallazgos y aspectos adicionales deben obtenerse después de la fluoroscopia para mayor detalle.

La fluoroscopia es uno de los métodos más importantes y satisfactorios para el examen del tórax.

### RESUME

La téléroadiographie thoracique se comporte comme un élément de "reconnaissance" pour la découverte des lésions intrathoraciques. Quand le diagnostic ne s'y inscrit pas, il y a lieu de continuer les investigations radiologiques. Dans la règle, il y a lieu de commencer par la radioscopie.

Un examen radioscopique valable pour la lésion thoracique comporte les recherches suivantes:

- 1 Observation des plus petits détails de la lésion
2. Rotation du malade derrière l'écran pour rechercher les relations entre la lésion et les éléments normaux voisins
- 3 Manoeuvre respiratoire pour mettre en évidence une participation vasculaire et pour préciser la localisation
- 4 Ingestion de baryte afin de préciser l'existence d'une lésion ou le déplacement du tractus gastro-intestinal
- 5 Examen du malade en diverses positions, afin de mettre en évidence l'effet de la pesanteur sur les lésions

La prise de clichés localisés au cours de l'examen radioscopique est essentielle pour permettre d'avoir un témoignage permanent des constatations faites, et afin de mettre en évidence de nouveaux détails.

La radioscopie est une des méthodes les plus importantes et les plus profitables dans l'examen radiologique du thorax.

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# Combined Action of Pas and Chloromycetin on Tubercle Bacilli\*

K C GUPTA, MD and R VISWANATHAN, MD, FCCP

Delhi, India

Combined action of different anti-tuberculosis drugs has been studied by various workers. Vennesland et al (1948) studied the combined action of streptomycin and para-aminosalicylic acid and Chopra and Gupta (1952) streptomycin and chloromycetin, Gupta and Chopra (1953) chloromycetin and pterogosperrin. Recently Hobby et al (1953) have reported that streptomycin and isoniazid act synergistically when used under appropriate condition in adequate quantities. The present study was undertaken to study the combined effect of PAS and chloromycetin.

PAS (Lehman 1946) is an active tuberculostatic drug which in conjunction with streptomycin delays the emergence of streptomycin resistant strains. Chloromycetin, Ehrlich et al (1947) possesses 10 times less anti-tuberculous activity than that of streptomycin.

Chloromycetin and PAS were used.

We used the same methods as described previously (Chopra and Gupta 1952).

TABLE I

Combined action of PAS and Chloromycetin against M tuberculosis								
Conc of PAS in ug/cc		Concentration of Chloromycetin in-ug/cc						
		0	10	5	2	1	0.5	0.2
0		3	0	1	3	3	3	3
10		0	0	0	0	0	0	0
8		1	0	0	0	1	1	1
5		2	0	0	1	2	2	2
2		3	0	0	1	2	2	2
1		3	0	0	1	2	2	2
5		3	0	0	1	3	3	3

Note

- 0 indicates no growth
- 1 slight growth
- 2 moderate growth
- 3 full growth

From table it is seen that the minimum inhibitory concentrations of PAS and chloromycetin alone are 10 ug/cc. When 8 ug/cc of PAS which inhibit the growth partially are used in combination with 5 ug/cc and 2 ug/cc of chloromycetin, there is complete inhibition of growth, while there is partial inhibition with 1 ug/cc, 0.5 ug/cc and 0.2 ug/cc of chloromycetin. The results when plotted graphically (Graph 1) according to the method of Eagle et al (1948) demonstrated that the drugs act synergistically.

\*From Vallabhbhai Patel Chest Institute, University of Delhi, Delhi

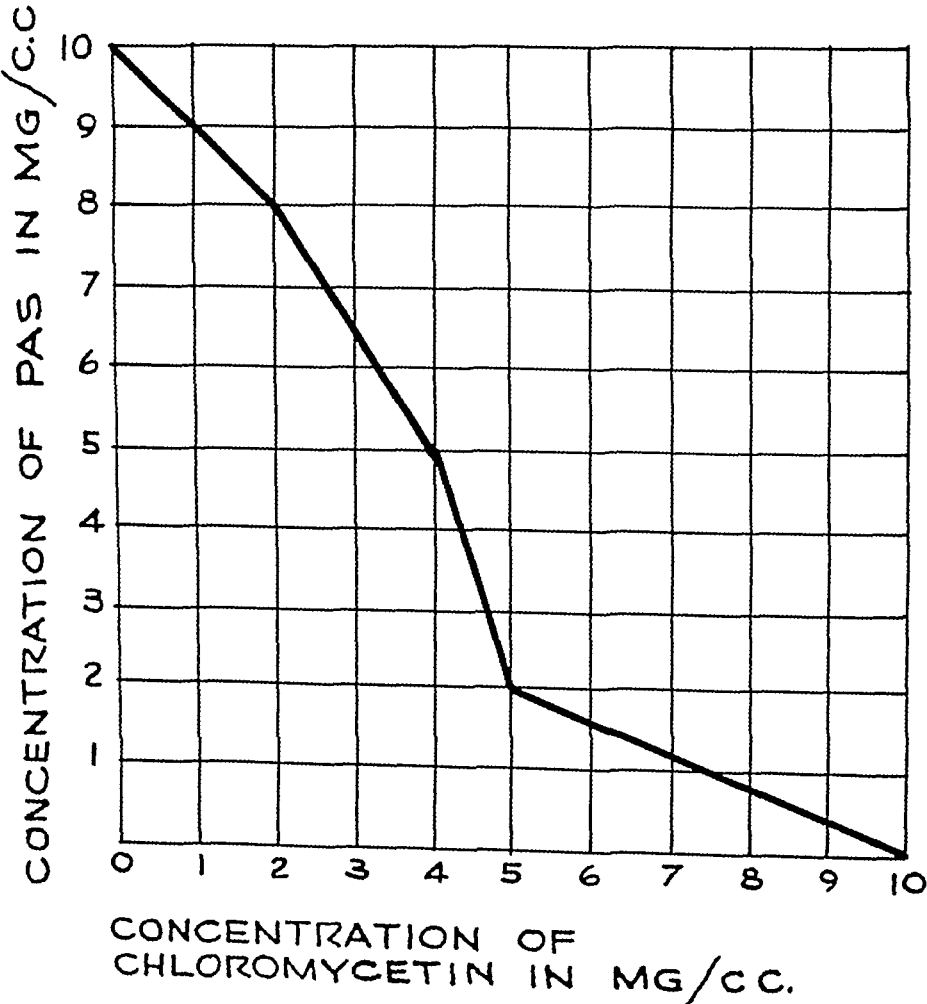
TABLE II

Combined action of PAS and Chloromycetin against bovine strain of M tuberculosis B19-3 (Kasauli)										
PAS in ug/cc	Chloromycetin in ug/cc									
	0	10	5	25	125	06	03	015	007	
0	3	0	1	1	2	3	3	3	3	
10	0	0	0	0	0	0	0	0	0	
6	1	0	0	0	0	0	1	2	2	
4	1	0	0	0	0	0	1	2	2	
2	2	0	0	0	0	1	2	2	2	
1	2	0	0	0	0	1	2	2	2	
05	3	0	0	0	1	2	3	3	3	

From the table it is seen that 10 ug/cc of PAS and 10 ug/cc of chloromycetin alone inhibit the growth, while 6 ug/cc of PAS and 5 ug/cc of chloromycetin cause partial inhibition

Six ug/cc of PAS when used in combination with 5 ug/cc, 25 ug/cc, 125 ug/cc and 06 ug/cc of chloromycetin result in complete inhibition There is partial inhibition with 03 ug/cc and 007 ug/cc of chloromycetin

GRAPH NO. I



The results when expressed graphically demonstrate that the combined action of PAS and chloromycetin is synergistic (Graph 2)

#### SUMMARY

Combined action of PAS and chloromycetin has been studied against Myco tuberculosis B19-4 (Human) and B19-3 (Bovine strains) and synergism has been demonstrated against these organisms

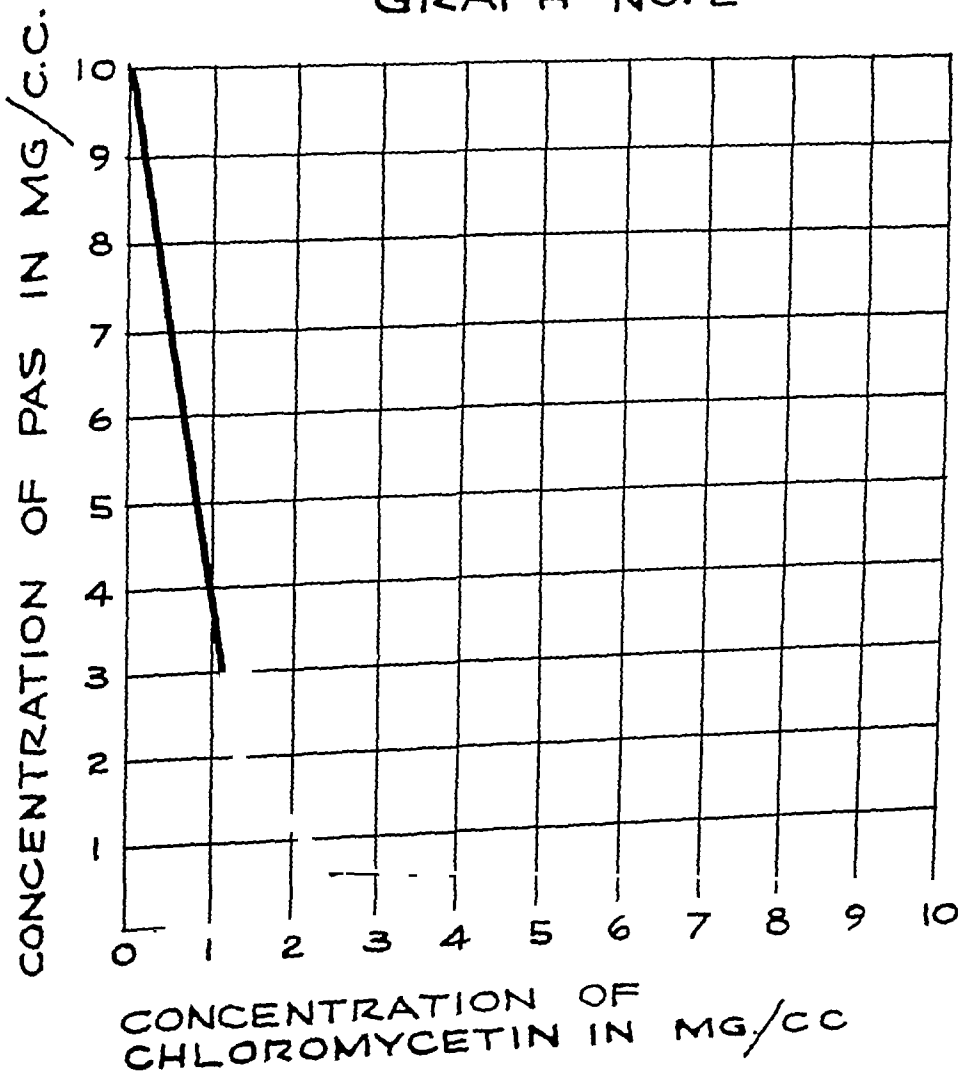
#### RESUMEN

Se ha estudiado la acción combinada del PAS y de la cloromicetina contra la cepa de micobacteria tuberculosa B19-3 (Bovina), y se ha demostrado sineigismo contra ambos organismos

#### RESUME

Les auteurs ont étudié l'action combinée de la chloromycétine et du PAS contre la bacille de la tuberculose. Ils ont particulièrement étudié cette action contre les souches B 19-4 (souche humaine) et B 19-3 (souche bovine). Ils ont démontré que cette association avait une action synergique contre ces microbes

GRAPH NO. 2



# Teaching Physical Diagnosis of the Chest

THEODORE H NOEHREN, M D, F C C P and JOSEPH B KOPP, M D \*

Buffalo, New York

Physical diagnosis of the chest is a dying art in this country. The information provided by skilled, available roentgenologic examination has insidiously replaced observation, palpation, percussion and auscultation as the basis for decisions in diagnosis, therapy and prognosis of many chest diseases. Perhaps this is truest for those of us who have been trained during the recent, exciting advances in laboratory methods. And yet, in our haste to employ a definitive procedure, we are vulnerable through neglect of this fundamental discipline—competent, painstaking, time consuming physical diagnosis.

All of us have studied cases in which physical diagnosis was the only accurate or available means of determining the cause of illness. Pneumonia, atelectasis, pulmonary edema, vascular anomalies and bronchial obstruction syndromes may be found by physical examination when chest x-ray films are not helpful. House officers frequently discard a diagnosis based on their physical diagnosis because roentgenograms fail to confirm their findings. Either their methods are faulty or they lack confidence in them. It can be a revealing experience to ask a student or house officer to demonstrate his concept of a complete physical examination of the chest, explaining the physiology and significance of his findings. Many of us might fare poorly also under such scrutiny. The need then, is for sounder instruction and more diligent practice of the art.

Two remedies for our fading physical diagnostic acuity are (1) performance of comfortable, careful, complete examination in all chest cases as an example to junior members of the medical echelon and (2) re-orientation of our methods in teaching physical diagnosis.

It is axiomatic that medical students learn most by observing their house staff and attending physicians. Despite the number of formal presentations, the third and fourth year students are more impressed by watching internes, residents and attendings. The interne also learns from his resident and from the exceptional physician who demonstrates to him findings that he has missed and the method whereby the findings are elicited. The entire echelon profits by contact with the clinician who continually demonstrates his proficiency with physical diagnosis. But the art suffers by lack of example and by the attitude propagated at ward rounds and chest conferences where examination of the patient is replaced by perusal of x-ray films. We cannot preach the theory of physical diagnosis and practice diagnosis by x-ray films without profoundly affecting our students. It might be better to replace formal lectures by more demonstrative lessons of everyday practice.

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\*Department of Medicine, University of Buffalo School of Medicine and Buffalo General Hospital

The third in a new series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians



A second, and chronologically earlier phase of teaching physical diagnosis is in the introductory course usually given during the second year of medical school. In some institutions this course is evolving into an introduction to internal medicine. This tendency is a natural consequence since, to understand physical findings, a knowledge of underlying dynamics is necessary. But, too often, with this approach, the patient supposedly representing a demonstration of physical findings, becomes an accessory to a discussion of disease problems. Young preceptors, whose finesse in physical diagnosis is often less than their medical acumen are most subject to this failing. A thoughtful reappraisal of each course is necessary to reorient methods to the purpose of the course.

Small groups, in which the major proportion of time is devoted to individual instruction with opportunities for practice on details of method, are effective. This approach starts with the normal subjects and utilizes repetition as the basic means to developing technique.

In the practice of a musical art or the development of athletic prowess, successful teachers devote what may seem disproportionate time to finger exercises, practice of the "correct" stroke, tackling the dummy, practicing footwork, exercises of balance and coordination. In an era when medical education has improved through application of the "learn by doing" concept, we can profit by the example of other areas where learning by doing demands rather tedious concentration on specific details.

Each student can learn best by thoroughly and repeatedly examining a classmate in a small, informal group. There is no substitute for the beginner doing it himself under the close scrutiny and criticism of his peers and their instructor. Most courses already include an hour or two of "normal" examination. However, if done correctly, this becomes a very time-consuming process, requiring more than one or two sessions in the course. The results so obtained prove that such individual instruction is necessary. To anticipate that later practice will compensate for deficiencies in technique during the learning period is the very fallacy which has produced our present problem.

The patient with abnormal physical findings must remain an important figure but is utilized for the application of techniques learned in the practice session. The students are thereby provided an opportunity to use methods they have been practicing and are introduced to abnormal findings on a background of experience with the normal. The student is encouraged to practice between classes to perfect his technique.

History taking is equally important in physical diagnosis and should receive the same individual instruction and attention.

Several ancillary lessons are taught by this approach. The students learn by experience the "feel" of a complete physical examination. Nothing else can impress upon them the subjective significance of such details as probing questions, uncomfortable positions, the nudity and inconvenience of examining gowns, clumsy technique, cold stethoscopes, cold hands and patient fatigue. Later finesse as a physician involves an appreciation of these reactions.

## The President's Page

The original purpose of the American College of Chest Physicians "to bring information concerning diseases of the chest to the physician" has been the prime objective of the Committee on Scientific Program for the 21st Annual Meeting of the College to be held June 2 through 5, with headquarters at the Ambassador Hotel, Atlantic City

During a recent visit to the College headquarters in Chicago, I had the opportunity to review the program, which appears in this issue of DISEASES OF THE CHEST. I am sure you will agree with me that it is one of the finest scientific programs of the College. The specialist in diseases of the chest and the research workers should find much to hold their attention throughout the meeting.

Some of the highlights of the program are the Selman Waksman Lecture, sponsored by the New Jersey Chapter of the College, the Fireside Conferences, panel discussions and round table luncheons. Motion picture sessions on diseases of the chest will be presented on each day of the meeting simultaneously with the scientific program. All of these special features combine to make your Atlantic City visit well worth while.

Dr. Irving Willner, Newark, New Jersey, Regent of the College, is serving as chairman of the Committee on General Arrangements for the meeting. Dr. Willner has announced that plans are progressing satisfactorily for an outstanding reunion in Atlantic City.

Thursday, June 2, will be devoted to administrative sessions and Fellowship Examinations. Councils and committees of the College will hold their annual meetings on that day. The Board of Regents and Board of Governors will meet jointly on Thursday morning, and the annual meeting of the Board of Regents will be held in the afternoon. These meetings are of prime importance to the College and its membership, as it is through the earnest and diligent work of its boards, its councils and its committees that the American College of Chest Physicians maintains its high standards and reputation for research and education in the field of diseases of the chest. I trust that every member of the College who is serving as a member of one of the councils or committees will make it a point to be present for the meetings and take an active part in the discussions. Members who are not serving on one of the councils or committees, but who have particular interest in the activities of any group, are cordially invited to join in the discussions.

The annual administrative session at which the reports of the Treasurer, Historian, Executive Director and Committee on Nominations will be received, is to be held at 9 a.m. on Saturday morning, June 4. Elections of officers of the College for the year 1955-1956 will take place at the administrative session.

On Saturday evening, June 4, the Annual Convocation of the College will be held, starting at 6:00 p.m. The cocktail party and Presidents' Banquet will follow and the evening will conclude with dancing and entertainment. Following the pattern set at our last annual meeting in San Francisco, there will be no speeches at the Annual Presidents' Banquet.

The Ladies Reception Committee, under the chairmanship of Mrs. Irving Willner, has prepared an attractive program. Will you please bring this program to the attention of your lady? We trust that she will accompany you to Atlantic City and participate in the ladies activities. Our ladies have been an inspiration to us and have added much to the success of our meetings. Mrs. Hudson and I are looking forward to the pleasure of seeing you and your lady at our 21st Annual Meeting.

*William A. Hudson*

## 21st ANNUAL MEETING PROGRAM

On the following pages we are pleased to present the scientific program for the 21st Annual Meeting of the American College of Chest Physicians, to be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1955. In organizing this program your committee made every effort to incorporate all aspects of diseases of the chest and still leave more than the usual amount of time for discussion.

In looking over the program, you will find many innovations which we trust will interest you. We wish to bring to your attention the Fireside Conferences, which are to be presented for the first time at this annual meeting. It has been the aim of the committee in organizing these Fireside Conferences, to make possible the discussion of a variety of timely topics. Our committee trusts that every member of the College will attend and participate in these conferences. They have been arranged so that everyone who wishes may take an active part in the discussion. A group of hosts will be on hand to direct the participants to the various tables. Informality and good fellowship will be the keynote of the evening's program.

The popular round table luncheons will be presented again this year. Many new subjects will be discussed by prominent scientists and, here again, there will be adequate time permitted for audience participation.

We call your special attention to the various symposia which have been organized for the meeting. The moderators of the panels have been alerted to make certain that these subjects are thoroughly discussed by the panelists and the audience.

The committee suggests that you complete the coupon for the luncheons you wish to attend and for the Presidents' Banquet. The demand for places at these functions is always far in excess of the number that can be accommodated. Our committee therefore urges that you please send in your reservations as soon as possible. You will also find a coupon for hotel reservations on page XXV.

Physicians who wish to enroll in the Seminars to be presented on Wednesday, June 1, should make application at an early date as facilities necessitate the acceptance of only a limited number. Preference, however, will be given to College members for these functions.

Our committee regrets that not all physicians who desired to participate in the 21st Annual Meeting of the College were able to be given places on the program. However, we do appreciate their interest in writing to us concerning their work.

The Committee wishes to express its thanks to the physicians who were kind enough to assist in the preparation of the scientific program and to the staff at the Executive Offices in Chicago whose assistance and cooperation have been invaluable.

### Committee on Scientific Program

Burgess L. Gordon, Philadelphia, Pennsylvania, *Chairman*

Albert H. Andrews, Jr., Chicago, Illinois, *Vice-Chairman*

Alvan L. Barach, New York, N. Y.

John F. Briggs, St. Paul, Minnesota

Sumner S. Cohen, Oak Terrace, Minnesota

Alfred Goldman, Beverly Hills, California

## SEMINARS

## Ambassador Hotel, Atlantic City

The following seminars on diseases of the chest will be presented at the Ambassador Hotel on Wednesday, June 1, and are open to all physicians. The seminars have been accredited by the Board of Examiners for candidates for Fellowship in the College and preference will be given to members.

The registration fee for each seminar, which consists of a series of four lectures, is \$7.50. Registration must be made in advance and accompanied by the tuition fee, seating capacity is limited and reservations will be accepted in the order received. A coupon for this purpose will be found opposite page 355. Please indicate your preference by number.

**Wednesday, June 1****Morning Sessions—9.00 a.m.—12.00 Noon****AM-1 Diagnosis of Non-Tuberculous Pulmonary Conditions**

*Moderator* Charles Hyman, Medical Director, Atlantic County Hospital for Tuberculous Diseases, Chief of Medical Service, Atlantic City Hospital, Atlantic City

- 9 00 a m "Advances in X-ray Diagnosis"  
Paul S. Friedman, Instructor in Radiology, University of Pennsylvania Graduate School of Medicine, Philadelphia
- 9 30 a m Question and answer period
- 9 45 a m "Bronchoscopic Approach in Diagnosis and Treatment"  
Charles M. Norris, Clinical Professor of Laryngology and Broncho-Esophagology, Department of Laryngology and Broncho-Esophagology, Chevalier Jackson Bronchoscopic Clinic, Temple University School of Medicine and Hospital, Philadelphia
- 10 15 a m Question and answer period
- 10 30 a m "Current Status of Hypersensitivity Diseases (Collegen Vascular Diseases)"  
Robert L. Mayock, Assistant Professor of Clinical Medicine (Diseases of the Chest), University of Pennsylvania School of Medicine, Philadelphia
- 11 00 a m Question and answer period
- 11 15 a m "Management of the Severe Asthmatic"  
Harry L. Rogers, Assistant Professor of Clinical Medicine, Jefferson Medical College, Physician-in-Charge, Allergy Out-Patient Department, Jefferson Hospital, Philadelphia
- 11 45 a m Question and answer period
- 12 00 noon Adjourn for lunch

**AM-2 The Physiologic Considerations of Pulmonary Disease**

*Moderator* Thomas J. E. O'Neill, Associate Professor of Thoracic Surgery, Hahnemann Medical College, Assistant Professor of Surgery, University of Pennsylvania Graduate School of Medicine, Philadelphia

- 9 00 a m "The Significance of Dyspnea"  
Roger H. L. Wilson, Clinical Instructor in Medicine, University of California Medical Center, San Francisco
- 9 30 a m Question and answer period
- 9 45 a m "Evaluation of Pulmonary Function Techniques"  
Richard L. Riley, Associate Professor of Environmental Medicine and Medicine, Johns Hopkins University School of Medicine and Hospital, Baltimore
- 10 15 a m Question and answer period
- 10 30 a m "Diagnostic Values of Cardiac Catheterization"  
Richard T. Cathcart, Associate Professor of Medicine, Jefferson Medical College, Philadelphia
- 11 00 a m Question and answer period
- 11 15 a m "Advances in Inhalation Therapy"  
Hylan A. Bickerman, Associate in Medicine, Columbia University College of Physicians and Surgeons, Research Fellow and Assistant Visiting, Columbia Research Service, New York City
- 11 45 a m Question and answer period
- 12 00 noon Adjourn for lunch

**Wednesday, June 1, Seminars (continued)****Afternoon Sessions—2:00 p.m.—5:00 p.m.****PM-1 Pulmonary Tuberculosis**

*Moderator* James S Edlin, Associate Clinical Professor of Medicine, New York Medical College, Tuberculosis Division, City Hospital, Manhattan General Hospital Tuberculosis Service, New York City

- 2 00 p m "The Selection of Anti-Microbial Drugs for Patients of Different Categories"  
Edward H Robitzek, Director of Medicine, Sea View Hospital, Staten Island Hospital, Staten Island
- 2 30 p m Question and answer period
- 2 45 p m "Present Status of Collapse Therapy, Medical and Surgical"  
Robert V Cohen, Assistant Professor of Medicine, Temple University School of Medicine, Philadelphia
- 3 15 p m Question and answer period
- 3 30 p m "Pulmonary Resection, Selection of Patients and Results"  
Herbert C Maier, Assistant Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons, Director of Surgery Lenox Hill Hospital, New York City
- 4 00 p m Question and answer period
- 4 15 p m "Comments on the Past and Present Methods of Prevention and Treatment"  
Jacob J. Kirshner, Associate in Medicine, Jefferson Medical College, Philadelphia, Medical Director, Eagleville Sanatorium, Eagleville, Pennsylvania
- 4 45 p m Question and answer period
- 5 00 p m Adjourn to visit exhibits

**PM-2 Cardiology**

*Moderator* Joseph Keiserman, Instructor in Medicine, Jefferson Medical College, Philadelphia

- 2 00 p m "The Use of Angiocardiography in Congenital Heart Disease"  
George P Keefer, Instructor in Radiology, University of Pennsylvania School of Medicine, Assistant Professor of Radiology, Woman's Medical College, Eva F Fox, Associate in Medicine, Clinical Instructor in Radiology, Hospital of the Woman's Medical College, Philadelphia
- 2 30 p m Question and answer period
- 2 45 p m "Pathologic Physiology of Hypertension"  
Louis A Soloff, Clinical Professor of Medicine, Temple University School of Medicine, Philadelphia
- 3 15 p m Question and answer period
- 3 30 p m "Management of Advanced Coronary Artery Disease"  
Samuel Bellet, Professor of Clinical Cardiology, University of Pennsylvania Graduate School of Medicine, Director, Division of Cardiology, Philadelphia General Hospital, Philadelphia
- 4 00 p m Question and answer period
- 4 15 p m "Newer Concepts in the Diagnosis and Treatment of Rheumatic Fever"  
William I Geffer, Associate Professor of Medicine, Woman's Medical College, Philadelphia
- 4 45 p m Question and answer period
- 5 00 p m Adjourn to visit exhibits

## SCIENTIFIC PROGRAM

### Thursday, June 2

#### 7 55 p m —Scientific Session

William A Hudson, President, American College of Chest Physicians,  
Detroit, Michigan, Chairman

James H Stygall, President-Elect, American College of Chest Physicians,  
Indianapolis, Indiana, Co-Chairman

#### 8 00 p m —“Evolution of the Chest Specialist”

Burgess L Gordon, Chairman, Committee on Scientific Program, American  
College of Chest Physicians, President and William J Mullen Professor of  
Medicine, Woman's Medical College, Philadelphia

#### 8 10 p m —The Selman Waksman Lecture

Sponsored by the New Jersey Chapter, American College of Chest  
Physicians

#### “Modern Concepts of Tuberculosis Therapy”

Sir Geoffrey Todd, Medical Superintendent, King Edward VII Sanatorium,  
Civilian Consultant in Diseases of the Chest to the Royal Air Force, Hon  
Consultant in Tuberculosis to the British Army, Consulting Physician to  
the Red Cross Hospital for Officers (Putney, London), Vice President,  
British Tuberculosis Association, Sussex, England

## Symposium

### “What is Causing the Increase of Cancer of the Lung?”

*Moderator* Edgar Mayer, Clinical Professor of Medicine, New York University  
Graduate School of Medicine, New York City

#### 8 30 p m Introduction

#### 8 35 p m “Disclosure of Cancer in X-ray Surveys”

Katharine R Boucot, Professor of Preventive Medicine and Clinical  
Professor of Medicine, Woman's Medical College, Chief, Division of  
Chronic Diseases of the Chest, Philadelphia General Hospital, Philadelphia

#### 8 50 p m “Is Cancer Due to Cigarette Smoking?”

Alton Ochsner, The William Henderson Professor of Surgery and Chairman  
of the Department of Surgery, Tulane University of Louisiana School of  
Medicine, Senior Visiting Surgeon and Surgeon-in-Chief, Tulane Surgical  
Service, Charity Hospital, Director, Section on Surgery, Ochsner Clinic  
and Ochsner Foundation Hospital, New Orleans

#### 9 05 p m “How About Air Pollution?”

John J Phair, Professor of Preventive Medicine, University of Cincinnati  
College of Medicine, Maurice L Thomson, Assistant Professor of Preventive  
Medicine, University of Cincinnati College of Medicine, Senior Lecturer (on  
leave), Department of Applied Physiology, London School of Hygiene and  
Tropical Medicine

#### 9 20 p m “The Anatomic Approach in Answer to the Question”

Oscar Auerbach, Chief, Laboratory Service, Veterans Administration  
Hospital, East Orange, N J, Associate Professor of Pathology, New York  
Medical College, New York City

#### 9 35 p m Panel discussion and questions from the floor

#### 10 10 p m Summarization by the moderator

#### 10 20 p m Adjournment

**Friday, June 3****8 55 a m —Scientific Session**

- 9 00 a m "Changes of Mechanics in Breathing in Different Body Positions"  
 Ernst O Attinger, Research Fellow in Medicine, Tufts College Medical School, Chief Resident, Department of Inhalational Therapy, Boston City Hospital, Maurice S Segal, Clinical Professor of Medicine, Tufts College Medical School, Director, Department of Inhalational Therapy, Boston City Hospital, Boston

- 9 10 a m "The Cough Hazard"  
 Andrew L Banyai, Associate Clinical Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin, Minas Joannides Jr, Senior Resident, Thoracic Surgical Service, Veterans Administration Hospital, Hines, Illinois

**Symposium on Pulmonary Emphysema**

*Moderator* Edwin R Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago

- 9 30 a.m. Introduction
- 9 35 a m "Clinical Aspects"  
 James Kieran, Clinical Instructor in Medicine (Diseases of the Chest), Stanford University School of Medicine, Oakland, California
- 9 55 a m "Disturbances of Cardio-Pulmonary Function"  
 Hurley L Motley, Professor of Medicine and Director, Cardio-Respiratory Laboratory, University of Southern California, Los Angeles
- 10 10 a m "The Role of the Diaphragm"  
 Coleman B Rabin, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York City
- 10 25 a m "Advances in Treatment"  
 Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Associate Attending Physician, Presbyterian Hospital, New York City
- 10 45 a m Panel discussion and questions from the floor
- 11 35 a m Summarization by the moderator
- 11 45 a m Adjourn to visit exhibits
- 12 00 noon **ROUND TABLE LUNCHEON DISCUSSIONS** (see pages 349, 350 and 351)

**2 00 p m —Scientific Session**

"The Silent Zone of the Human Heart"  
 Myron Prinzmetal, Associate Professor of Medicine, University of California, Chief of Cardiology, City of Hope Hospital, Attending Physician, Cedars of Lebanon Hospital, Alfred Goldman, Chief of Professional Services, City of Hope Medical Center, Duarte, Chief, Thoracic and Cardiac Surgery, Cedars of Lebanon Hospital, Rashid A Massumi, Research Associate, Cedars of Lebanon Hospital, Louis Rakita, Research Associate, Cedars of Lebanon Hospital, Los Angeles

**Friday, June 3 (continued)****Symposium on Cardiac Manifestations in Chronic Pulmonary Disease**

*Moderator* John F Briggs, Associate Professor of Clinical Medicine,  
University of Minnesota Medical School, Minneapolis

2 20 p m Introduction

2 25 p m "Physiopathology"

Julius H Comroe, Jr, Professor and Chairman, Department of Physiology and Pharmacology, University of Pennsylvania Graduate School of Medicine, Isaac Ott, Professor of Physiology and Pharmacology, University of Pennsylvania Graduate School of Medicine, Philadelphia

2 40 p m "Evaluation of Cardiac Function and Disability"

Irving Mack, Clinical Assistant Professor of Medicine, Chicago Medical School, Associate Attending Physician, Chest Department, Michael Reese Hospital and Winfield Hospital, Research Associate, Department of Cardiovascular Research, Michael Reese Hospital, Chicago

2 55 p m "Special Physiologic Treatment"

Simon Dack, Lecturer in Medicine, Columbia University College of Physicians and Surgeons, Chief of the Cardiac Clinic, Mt Sinai Hospital, New York City

3 10 p m "General Cardiac Treatment"

Arthur M Master, Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Cardiologist, Mt Sinai Hospital, New York City

3 25 p m Panel discussion and questions from the floor

4 20 p m Summarization by the moderator

4 30 p m Adjourn to visit exhibits

8 15 p m —Scientific Session

**"Fireside Conferences"****Hosts**

Albert H Andrews Jr, Chicago, Illinois  
Carl C Aven, Atlanta, Georgia  
B Guy Begin, Montreal, Canada  
Otto L Bettag, Chicago, Illinois  
John F Briggs, St. Paul, Minnesota  
John S Chapman, Dallas, Texas  
Dean B Cole, Richmond, Virginia  
Seymour M Farber, San Francisco, Calif  
M Jay Flipse, Miami, Florida  
Carl H Gellenthien, Valmora, New Mexico  
Alfred Goldman, St Louis, Missouri  
Edward A Greco, Portland, Maine  
Alvis E Greer, Houston, Texas  
Edward W Hayes, Monrovia, California  
Willard B Howes, Detroit, Michigan  
William A Hudson, Detroit, Michigan  
Hollis E Johnson, Nashville, Tennessee

Harold I Kinsey, Toronto, Canada  
Donald R McKay, Buffalo, New York  
Herman J Moersch, Rochester, Minnesota  
Foster Murray, Brooklyn, New York  
Antonio Navarrete, Havana, Cuba  
James M Odell, The Dalles, Oregon  
William E Ogden, Toronto, Canada  
J Winthrop Peabody, Washington, D C  
Charles K Petter, Waukegan, Illinois  
Joseph C Placak, Cleveland, Ohio  
Jame F Pou, Hato Rey, Puerto Rico  
Alfred A Richman, New York, N Y  
Frederick Slyfield, Seattle, Washington  
James H Stygall, Indianapolis, Indiana  
W C Voorsanger, San Francisco, Calif  
David H Waterman, Knoxville, Tennessee  
Irving Willner, Newark, New Jersey



**Friday, June 3, Fireside Conferences (continued)****Subjects and Discussion Leaders****"Emphysema"**

Alvan L. Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Associate Attending Physician, Presbyterian Hospital, New York City

**"Coronary Artery Disease Surgery"**

Charles P. Bailey, Professor and Head of the Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia

**"Fungus Infection"**

Andrew L. Banyai, Associate Clinical Professor of Medicine, Marquette University School of Medicine, Milwaukee, Wisconsin

**"Angiocardiography"**

Israel Steinberg, Assistant Clinical Professor of Medicine and Radiology, Cornell University Medical College, Assistant Radiologist, New York Hospital, Consultant, Veterans Administration Hospital, New York City,  
Charles T. Dotter, Professor of Radiology and Head, Department of Radiology, University of Oregon Medical School, Hospitals and Clinics, Portland

**"Chemotherapy"**

Karl H. Pfuetze, Clinical Professor of Medicine, University of Illinois College of Medicine, Medical Director and Superintendent, Chicago State Tuberculosis Sanatorium, Chicago

**"Ambulatory Treatment in Tuberculosis"**

George G. Ornstein, Associate Professor of Medicine, New York Medical College, Professor of Medicine (Chest Diseases), New York Polyclinic Hospital Medical School, New York City

**"Endocavitary Aspiration"**

Vincenzo Monaldi, Director, Institute Principi di Piemonte, University of Naples, Antonio Blasi, Institute Principi di Piemonte, Naples, Italy

**"Asthma in Children"**

Bret Ratner, Professor of Clinical Pediatrics and Head of Pediatric Allergy, New York Medical College, Director of Pediatrics, Sea View Hospital, New York City

**"The Congenital Heart"**

Daniel F. Downing, Associate Professor of Pediatrics, Hahnemann Medical College, Philadelphia

**"Collapse Therapy"**

Harold G. Trimble, Associate Clinical Professor of Medicine (Diseases of the Chest), Stanford University School of Medicine, Oakland

**"Bronchoesophagology"**

Chevalier L. Jackson, Professor and Head of the Department of Laryngology and Bronchoesophagology, Temple University School of Medicine, Philadelphia

**"Esophageal Management"**

Arthur S. W. Touroff, Clinical Professor of Surgery, Columbia University College of Physicians and Surgeons, New York City

**"Extrapleural Pneumothorax"**

Donato G. Alarcon, Professor of Clinical Medicine, National University of Mexico, Director, Sanatorium San Angel, Mexico City

**"Bronchiectasis"**

Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago

**"Inoperable Carcinoma of the Lung"**

Edgar Mayer, Clinical Professor of Medicine, New York University Graduate School of Medicine, New York City

**"Pulmonary Edema"**

Aldo A. Luisada, Associate Professor of Medicine, Chicago Medical School, Director, Division of Cardiology, Chicago Medical School and Mt. Sinai Hospital, Chicago

**"Immunity and Vaccination in Tuberculosis"**

Jay Arthur Myers, Professor of Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Chief, Tuberculosis Service, Minneapolis General Hospital, Minneapolis

**Friday, June 3, Fireside Conferences (continued)****"Surgery in Lung Tumors"**

Richard H Overholt, Clinical Professor of Surgery (Thoracic), Tufts College Medical School, Director, Overholt Thoracic Clinic, Boston

**"Rheumatic Heart Disease"**

Arthur M Master, Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Cardiologist, Mt Sinai Hospital, New York

**"Rehabilitation in Pulmonary Disease"**

David A Cooper, Professor of Clinical Medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia

**"Cardiac Function"**

John J Sampson, Clinical Professor of Medicine, University of California School of Medicine, Chief of the Department of Medicine, Mt Zion Hospital, San Francisco

**"Surgery of Heart Valves"**

Dwight E Harken, Associate Clinical Professor of Surgery, Harvard University Medical School, Surgeon, Peter Bent Brigham Hospital, Boston

**"Excision in Tuberculosis"**

J Maxwell Chamberlain, Associate in Surgery, Columbia University College of Physicians and Surgeons, Attending in Charge of Thoracic Surgery, Roosevelt Hospital, New York City

**"Pathology of Resected Lesions"**

Henry C Sweany, Director of Research, Pathology and Allied Sciences, Missouri State Sanatorium, Mt Vernon,  
Hawley H Seiler, Director and Thoracic Surgeon, Tampa Tumor Clinic, Consultant, Thoracic Surgery, Veterans Administration Regional Office, Tampa

**"Pressure Breathing"**

Maurice S Segal, Clinical Professor of Medicine, Tufts College Medical School, Director, Department of Inhalation Therapy, Boston City Hospital, Boston

**"Asthma"**

Leon Unger, Associate Professor of Medicine, Northwestern University Medical School, Attending Physician, Cook County and Wesley Memorial Hospitals, Chicago

**"Pulmonary Function"**

George R Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, Director, Research Laboratory and Radioisotope Unit, Veterans Administration Hospital, Nashville

**"Aerosols"**

Max S Sadove, Professor of Anesthesiology and Head of the Division in Department of Surgery, University of Illinois College of Medicine, Head, Division of Anesthesiology, Research and Educational Hospitals, University of Illinois, Chicago

**"Coin Shadows"**

Alfred Goldman, Chief of Professional Services, City of Hope Medical Center, Duarte, Chief of Thoracic and Cardiac Surgery, Cedars of Lebanon Hospital, Los Angeles

**"Rehabilitation in Cardiac Disease"**

Nathaniel E Reich, Clinical Assistant Professor of Medicine, State University of New York College of Medicine, Associate Cardiologist, Jewish Sanatorium and Hospital for Chronic Diseases, Brooklyn, New York

**"Dust Diseases"**

Louis L Friedman, Consultant in Chest Diseases, Veterans Administration, Tuscaloosa, South Highlands Infirmary, Jefferson-Hillman Hospital, Birmingham, Ala

**"Positions and Incisions in Thoracic Surgery"**

Emil A Naclerio, Chief, Thoracic Surgical Services, Harlem and Columbus Hospitals, New York City

**NOTE**

These conferences are informal and offer an opportunity for free discussion of many subjects of interest to our members. Discussion Leaders will be seated at tables with proper identification. Physicians may participate in the discussion of their choice, or move on to other discussions when and if they desire. Refreshments will be served to enhance good fellowship.

**Saturday, June 4****9 55 a m —Scientific Session, Section I****Unrelated Papers on Pulmonary Diseases with Special Reference to  
Techniques for Diagnosis and Treatment**

*Moderator* Sumner S Cohen, Assistant Medical Director, Glen Lake Sanatorium,  
Oak Terrace, Instructor, University of Minnesota, Minneapolis

10 00 a m *Introduction*

10 05 a m "Clinical and Laboratory Observations in Enzymatic Therapy"  
Seymour M Farber, Associate Clinical Professor of Medicine, University  
of California School of Medicine, David A Wood, Director, Cancer Re-  
search Institute, Samuel L Pharr, Cancer Research Institute, John K  
Frost, Instructor in Pathology, University of California Medical School,  
San Francisco

10 15 a m "Intermittent Positive Pressure Therapy in Pediatrics"  
Roy F. Goddard, Director, Pediatrics Research Laboratory, The Lovelace  
Foundation, Albuquerque, New Mexico

10 25 a m "Modern Therapy and Rehabilitation in Tuberculosis"  
Richard R Trail, Medical Director, Papworth and Enhamalamein Village  
Settlements, London, England

10.35 a m Questions from the floor

10 50 a m "Tuberculosis and Pregnancy"  
Hollis E Johnson, Associate Professor of Clinical Medicine, Vanderbilt  
University School of Medicine, Nashville

11 00 a m "An Optimistic View of Surgery in Primary Cancer of the Lung"  
Richard H Overholt, Clinical Professor of Surgery (Thoracic), Tufts  
College Medical School, Thoracic Surgeon, New England Deaconess  
Hospital, Director, Overholt Thoracic Clinic, James Bougos, Overholt  
Thoracic Clinic, Boston

11 10 a m "The So-Called Tuberculoma A Reappraisal"  
J Winthrop Peabody, Jr., Instructor in Thoracic Surgery, Georgetown  
University School of Medicine, Edgar W. Davis, Professor of Thoracic  
Surgery, Georgetown University School of Medicine, Sol Katz, Adjunct  
Clinical Professor of Medicine, Georgetown University School of Medicine  
and George Washington Medical School, Chief, Division of Pulmonary  
Diseases, Department of Public Health, Washington, D C

11 20 a m Questions from the floor

11 40 a m Summarization by the moderator

11 45 a m Adjourn to visit exhibits

**9 55 a m —Scientific Session, Section II****Symposium on Cardiac Surgery**

*Moderator* Charles P Bailey, Professor and Head of the Department of Thoracic  
Surgery, Hahnemann Medical College, Director, Bailey Thoracic Clinic, Philadelphia

10 00 a m "The Surgery of Patent Ductus and Coarctation of the Aorta"  
David H Waterman, Chief, Thoracic Surgery, Fort Sanders Presbyterian  
Hospital, Attending Thoracic Surgeon, East Tennessee Tuberculosis Hos-  
pital, Knoxville General Hospital, Knoxville, William K Rogers, Attend-  
ing Thoracic Surgeon, Fort Sanders Presbyterian Hospital, Knoxville  
General Hospital, East Tennessee Tuberculosis Hospital, Knoxville,  
Tennessee

10 10 a m "Tetralogy of Fallot and Pulmonic Stenosis"  
John Storer, Director of the Department of Thoracic and Cardiovascular  
Surgery, Huron Road Hospital, East Cleveland

10 20 a m "Interatrial Septal Defects"  
Robert E Gross, William E Ladd Professor of Child Surgery, Head of the  
Department, Children's Hospital, Harvard University Medical School,  
Boston

**Saturday, June 4 (continued)**

- 10 30 a m "Surgery of Mitral and Aortic Stenosis"  
Julian Johnson, Professor of Surgery, University of Pennsylvania School of Medicine and Graduate School of Medicine, Philadelphia
- 10 40 a m "Open Cardiac Surgery a) Hypothermia, b) Heart-Lung Apparatus, c) Cross-Circulation"  
John H. Gibbon, Jr., Professor of Surgery and Director of Surgical Research, Department of Surgery, Jefferson Medical College, Philadelphia
- 10 50 a m Panel discussion and questions from the floor
- 11 35 a m. Summarization by the moderator
- 11 45 a m Adjourn to visit exhibits
- 12 00 noon **ROUND TABLE LUNCHEON DISCUSSIONS** (see pages 349, 350 and 351)

1 55 p m —Scientific Session, Section I

**Symposium****Is Tuberculosis in the Bag?**

*Moderator* Karl H. Pfuete, Clinical Professor of Medicine, University of Illinois College of Medicine, Medical Director and Superintendent, Chicago State Tuberculosis Sanatorium, Chicago

2 00 p m *Introduction*

2 05 p m "Is the Virulence of the Tubercle Bacillus Changing?"  
Emil Bogen, Clinical Associate Professor, Department of Infectious Diseases, University of California (Los Angeles), Head Pathologist, Olive View Sanatorium, Olive View, California

2 15 p m "Antimicrobial Therapy in Tuberculosis Dosage, Resistance, and Termination of Treatment"  
James A. Wier (Col.), Chief, Pulmonary Disease Service, Fitzsimons Army Hospital, Denver

2 25 p m "The Use of Cycloserine in the Treatment of Pulmonary Tuberculosis in Humans"  
Israel G. Epstein, Associate Clinical Professor of Medicine, New York Medical College, Assistant Director, Visiting Physician, Tuberculosis Service, Metropolitan Hospital, New York City

2 35 p m "The Long-Term Results of Thoracoplasty Resection"  
J. Maxwell Chamberlain, Associate in Surgery, Columbia University College of Physicians and Surgeons, Director of Surgery, Brooklyn Thoracic Hospital, New York City

2 50 p m Panel discussion and questions from the floor

3 15 p m Summarization by the moderator

3 20 p m Adjourn to visit exhibits

3 35 p m **The Future of the Tuberculosis Sanatorium**

Panel Discussion and Questions from the Floor

*Moderator* W. Edward Chamberlain, Professor and Head of the Department of Radiology, Temple University School of Medicine, Philadelphia

*Panel*

Robert J. Anderson, Assistant Chief, Division of Special Health Services, U. S. Public Health Service, Washington, D. C.  
Benson Bloom, Staff, Tucson Medical Center and St. Mary's Hospital and Sanatorium, Tucson, Arizona

Edward W. Hayes, Associate Professor of Thoracic Diseases, College of Medical Evangelists and Medical Director, Maryknoll Sanatorium, Monrovia, California

Royal H. McCutcheon, Deputy Medical Director, Pennsylvania State Sanatorium, Hamburg, and Consultant, Diseases of the Chest, St. Luke's Hospital, Bethlehem, Pennsylvania

Arthur B. Robins, Director, Bureau of Tuberculosis, New York City Department of Health, Visiting Physician, Triboro Hospital, New York City

4 35 p m Adjourn to visit exhibits

**Saturday, June 4 (continued)**

1 55 p m —Scientific Session, Section II

**Symposium****Cardiovascular Research with Special Reference to Treatment**

*Moderator* William Likoff, Associate Professor of Medicine, Hahnemann Medical College, Cardiologist, Bailey Thoracic Clinic, Philadelphia

2 00 p m *Introduction*

2 05 p m "Treatment of Cardiac Arrhythmias with Grave Prognostic Import"  
George E Burch, Henderson Professor and Chairman of the Department of Medicine, Tulane University School of Medicine, Physician and Chief, Division of Medicine, Tulane Unit, Charity Hospital, New Orleans

2 20 p m *Discussor* H Easton McMahon, Assistant Clinical Professor of Medicine, New York Medical College, Lecturer (Cardiology), New York Polytechnic Post Graduate Medical School, New York City

2 25 p m "Comparative Effects of Various Digitalis Glucosides in Heart Disease"  
Aldo A Luisada, Associate Professor of Medicine, Director of the Division of Cardiology, Chicago Medical School, Christ Aravanis, Research Assistant, Luigi Cardi, Research Assistant, Chicago Medical School, Chicago

2 40 p m *Discussor* Arthur Grishman, Instructor in Cardiology, Columbia University College of Physicians and Surgeons, Mt Sinai Hospital, New York City

2 45 p m "The Over-Treatment of Apparent Sodium and Potassium Imbalance"  
Isidore S Edelman, Associate Professor of Medicine, University of California School of Medicine, San Francisco

3 00 p m *Discussor* Harry L Jaffe, Lecturer in Medicine, Columbia University College of Physicians and Surgeons, Assisting Attending Physician (Cardiology), Mt Sinai Hospital, New York City

3 05 p m Summarization by the moderator

3 20 p m "Medical Therapy of Occlusive Arterial Disease"  
Walter F Kvale, Consultant, Department of Medicine, Mayo Clinic, Associate Professor of Medicine, Mayo Foundation Graduate School, University of Minnesota, Rochester

3 35 p m *Discussor* Hilton S Read, Director, Intern and Resident Training, Atlantic City Hospital, and Ventnor Diagnostic Center, Atlantic City

3 40 p m "The Techniques and Value of Vocational Guidance and Placement for the Cardiac Patient"  
Herman K Hellerstein, Clinical Instructor of Medicine, Western Reserve University School of Medicine, Assistant Physician, University Hospitals of Cleveland

3 55 p m *Discussor* William I Geffer, Associate Professor of Medicine, Woman's Medical College, Philadelphia

4 00 p m "Rehabilitation of the Cardiac Patient with Moderate Physical Limitations"  
Abraham Jezer, Associate Professor of Clinical Medicine, Albert Einstein College of Medicine, Attending Physician, Montefiore Hospital, Staff, Altro Workshops, New York City

4 15 p m *Discussor* Joseph Keiserman, Instructor in Medicine, Jefferson Medical College, Philadelphia

4 20 p m Summarization by the moderator

4 30 p m Adjourn to visit exhibits

**Sunday, June 5**

8 55 a m—Scientific Session

**Symposium****Occupational Influences in Diseases of the Chest**

*Moderator* Edward C Holmblad, Managing Director, Industrial Medical Association,  
Senior Attending Surgeon, St Luke's Hospital, Chicago

9 00 a m *Introduction*

9 05 a m "Characteristic Pathology of the Lungs"

Gerritt W H Schepers, Director, The Saranac Laboratory, Saranac Lake,  
New York

9 20 a m "The Heart"

Richard S Gubner, Associate Director of Medical Research, The Equitable  
Life Assurance Company, New York City

9 35 a m "Estimation of Disability and Employability"

Oscar A Sander, Associate in Medicine, Marquette University Medical  
School, Milwaukee County Hospital and Columbia Hospital, Milwaukee

9 50 a m Panel discussion and questions from the floor

10 15 a m Summarization by the moderator

10 20 a m Adjourn to visit exhibits

10 30 a m **Lecture Series on Chest Diseases and Related Problems**

*Moderator* John J Sampson, Clinical Professor of Medicine, University of California,  
Chief of the Department of Medicine, Mt Zion Hospital, San Francisco

10 30 a m *Introduction*

10 35 a m "Stimulating Opportunities for Research in Diseases of the Chest"

Herman J Moersch, Professor of Medicine, Mayo Foundation Graduate  
School, University of Minnesota, Chairman, Section of Internal Medicine,  
Mayo Clinic, Rochester

10 45 a m "The Responsibility of the General Thoracic Surgeon in Cardiac Surgery"

David J Dugan, Clinical Instructor in Surgery, Stanford University  
School of Medicine, Oakland, California

10 55 a m "Pheochromocytoma, Factors in the Accurate Pharmacologic Diagnosis"

Grace M Roth, Consultant, Department of Physiology, Associate  
Professor of Experimental Medicine (Mayo Foundation), Mayo Clinic,  
Walter F Kvale, Consultant, Department of Medicine, Mayo Clinic, Asso-  
ciate Professor of Medicine, Mayo Foundation Graduate School, University  
of Minnesota Rochester

11 10 a m "The Management of Intractable Angina Pectoris"

George R Herrmann, Professor of Internal Medicine, Director,  
Cardiovascular Research Laboratory, Director, Heart Station, University  
of Texas Medical Branch, Galveston

11 25 a m "How Effective are the Antibiotics against Tuberculosis?"

Edward Dunner, Chief, Training and Standards, Tuberculosis Service,  
U S Veterans Administration, Washington, D C

11 40 a m Summarization by the moderator

11 45 a m Adjourn to visit exhibits

12 00 noon **ROUND TABLE LUNCHEON DISCUSSIONS** (see pages 349, 350 and 351)

1 55 p m—Scientific Session

**Lecture Series on Chest Diseases and Related Problems (continued)**

*Moderator* David B Radner, Assistant Professor of Medicine, Chicago Medical School,  
Director, Chest Department, Michael Reese Hospital, Chicago, Medical Director,  
Winfield Sanatorium, Winfield, Illinois

2 00 p m *Introduction*2 05 p m "Severe Crushing Injuries of the Chest A New Method of Treatment  
with Continuous Hyperventilation by Means of Intermittent Positive  
Endotracheal Insufflation"

Edward E Avery, Associate in Surgery, Northwestern University Medical  
School, Ernst T Morch, Professor of Anesthesiology, University of Chi-  
cago School of Medicine, Jerome R. Head, Assistant Professor of Surgery,  
Northwestern University Medical School, Donald W Benson, Instructor in  
Anesthesiology, University of Chicago School of Medicine, Chicago

**Sunday, June 5 (continued)**

- 2:15 p m "Physiological and Clinical Changes Following Closure of Atrial Septal Defects"  
 Harry Goldberg, Assistant Professor of Medicine and Director, Cardio-Pulmonary Laboratory, Hahnemann Medical College and Hospital,  
 Daniel F. Downing, Associate Professor of Pediatrics, Hahnemann Medical College, Philadelphia
- 2:30 p m "Surgery and Supervoltage X-Ray Therapy of Cancer of the Lung"  
 David P. Boyd, Thoracic Surgeon, Lahey Clinic, New England Baptist and New England Deaconess Hospitals, Carlton R. Souders, Staff, Lahey Clinic, Magnus I. Smedel, Staff, Lahey Clinic, Boston
- 2:40 p m "Tuberculosis Among Nurses"  
 Jay Arthur Myers, Professor of Medicine and Public Health, University of Minnesota Medical and Graduate Schools, Chief, Tuberculosis Service, Minneapolis General Hospital, Minneapolis
- 2:55 p m Discussion and questions from the floor
- 3:15 p m Summarization by the moderator
- 3:25 p m Recess

**3:30 p m Diagnostic-Treatment Conference**

*Moderator* Peter A. Theodos, Associate in Medicine, Jefferson Medical College, Chief, Diagnostic Clinic, Barton Memorial Division, Jefferson Medical College Hospital, Clinical Chief, Division of Tuberculosis, City of Philadelphia

*Panel***Internist (pulmonary)**

Harold G. Trimble, Associate Clinical Professor of Medicine (Diseases of the Chest), Stanford University School of Medicine, Oakland, California

**Internist (cardiology)**

George R. Herrmann, Professor of Internal Medicine, Director, Cardiovascular Research Laboratory, Director, Heart Station, University of Texas Medical Branch, Galveston

**Pathologist (cardiology)**

Peter A. Herbut, Professor of Pathology and Head of the Department, Director of Clinical Laboratories, Jefferson Medical College and Hospital, Philadelphia

**Physiologist**

George R. Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, Director, Research Laboratory and Radioisotope Unit, Veterans Administration Hospital, Nashville

**Roentgenologist**

Jacob H. Vastine, II, Professor of Radiology, Woman's Medical College, Associate Professor of Radiology, University of Pennsylvania Graduate School of Medicine, Philadelphia

**Bronchoscopist**

Albert H. Andrews, Jr., Clinical Assistant Professor of Broncho-Esophagology, Department of Otolaryngology, University of Illinois College of Medicine, Chicago

**Surgeon (heart)**

Alfred Goldman, Chief of Professional Services, City of Hope Medical Center, Duarte, Chief, Thoracic and Cardiac Surgery, Cedars of Lebanon Hospital, Los Angeles

**Surgeon (lungs)**

Wilford B. Neptune, Associate, Overholt Thoracic Clinic, Staff Member, New England Deaconess Hospital, Carney Hospital, Cambridge City Hospital, Consultant, Brooklyn Veterans Hospital, New England Hospital, Boston

The moderator will lead the discussion on two selected cases, one dealing basically with a pulmonary problem, and the other cardiac. The cases selected will represent problems commonly encountered in clinical practice and will afford an opportunity for lively discussion. The panel will have been given only a few pertinent facts in advance and each case will be presented as if currently under treatment. As the case unfolds, discussion will ensue as to the probable diagnosis, treatment and errors of omission or commission. Discussion from the floor will be invited.

**ROUND TABLE LUNCHEONS****Friday, June 3****A-1 "Management of the Emphysematous Patient with Bronchial Asthma"**

Ethan Allan Brown, Associate Professor of Pediatrics, Tufts College Medical School, Physician-in-Chief, Allergy Section, Boston Dispensary, New England Medical Center, Boston,

A H Russakoff, Associate Professor of Clinical Medicine, Medical College of Alabama, Acting Chief of Tuberculosis, Veterans Hospital, Birmingham

*Moderator* Alvan L Barach, Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Associate Attending Physician, Presbyterian Hospital, New York City

**A-2 "Pulmonary Mycosis"**

Michael L Furcolow, Associate Clinical Professor of Medicine, University of Kansas School of Medicine, Medical Director and Medical Officer in Charge, University of Kansas Medical Center, Kansas City, Kansas,

Alvis E Greer, Clinical Professor of Medicine, Baylor University College of Medicine, Houston, Texas

*Moderator* David J Reisner, Visiting Physician, Sea View Hospital, Consulting Physician, Hospitals of the Department of Correction, New York City

**A-3 "Management of Tuberculosis in the Elderly Patient"**

Kenneth G Bulley, Medical Director and Superintendent, Kane County Springbrook Sanitarium, Aurora, Illinois,

Sol Katz, Chief, Division of Pulmonary Diseases, Department of Public Health, District of Columbia General Hospital, Adjunct Clinical Professor of Medicine, Georgetown University School of Medicine, and George Washington Medical School, Washington, D C

*Moderator* Harold G Trimble, Associate Clinical Professor of Medicine (Diseases of the Chest), Stanford University School of Medicine, Oakland, California

**A-4 "Pulmonary Complications in General Surgery"**

Henry L Dorfmann, Senior Clinical Chest Physician, Mt Sinai Hospital, Attending Physician, Gouverneur Hospital, New York City,

Max S Sadove, Professor of Anesthesiology and Head of the Division in the Department of Surgery, University of Illinois College of Medicine, Head, Division of Anesthesiology, Research and Educational Hospitals, University of Illinois, Senior Consultant in Anesthesiology, Veterans Hospital, Hines, Illinois,

Peter A Theodos, Associate in Medicine, Jefferson Medical College, Chief, Diagnostic Clinic, Barton Memorial Division, Jefferson Medical College Hospital, Clinical Chief, Division of Tuberculosis, City of Philadelphia

*Moderator* Edward M Kent, Associate Professor of Surgery, University of Pittsburgh School of Medicine, Pittsburgh

**A-5 "Bronchogenic Carcinoma: What Should be Done with the Suspect Cases?"**

Jonathan F Meakins, Lecturer, McGill University, Associate Physician, Royal Victoria Hospital, Montreal, Canada,

Richard H Overholt, Clinical Professor of Surgery (Thoracic), Tufts College Medical School, Thoracic Surgeon, New England Deaconess Hospital, Director, Overholt Thoracic Clinic, Boston

*Moderator* David Ulmar, Associate Clinical Professor of Medicine, New York University Post Graduate Medical School, New York City

**A-6 "Pericarditis"**

George R Herrmann, Professor of Internal Medicine, Director, Cardiovascular Research Laboratory, Director, Heart Station, University of Texas Medical Branch, Galveston,

William H Thomas, Assistant Clinical Professor of Medicine, University of California School of Medicine, San Francisco

*Moderator* William Likoff, Associate Professor of Medicine, Hahnemann Medical College, Cardiologist, Bailev Thoracic Clinic, Philadelphia



**Saturday, June 4****B-1 "Mass X-Ray Surveys, A Review of their Strength and Faults"**

Edward A. Piszczek, Associate Professor and Chairman of the Department of Preventive Medicine and Public Health, Stritch School of Medicine of Loyola University, Associate Professor of Public Health, University of Illinois College of Medicine, Executive Director, Suburban Cook County Tuberculosis Sanitarium District, Chicago,

Clarence M. Sharp, Director, Bureau of Tuberculosis Control, Florida State Board of Health, Consultant in Chest Diseases, Duval Medical Center, Jacksonville

*Moderator* Robert J. Anderson, Assistant Chief, Division of Special Health Services, U. S. Public Health Service, Washington, D. C.

**B-2 "Pressure Breathing Therapy, Positive and Negative Techniques"**

Hurley L. Motley, Professor of Medicine and Director, Cardio-respiratory Laboratory, University of Southern California, Los Angeles,

Maurice S. Segal, Clinical Professor of Medicine, Tufts College Medical School, Director, Department of Inhalation Therapy, Boston City Hospital, Boston

*Moderator* George R. Meneely, Associate Professor of Medicine, Vanderbilt University School of Medicine, Director, Research Laboratory and Radioisotope Unit, Veterans Administration Hospital, Nashville

**B-3 "Radioisotopes in Pulmonary Disease"**

R. Drew Miller, Consultant in Internal Medicine and Diseases of the Chest, Mayo Clinic and Rochester Methodist Hospital, Instructor, Mayo Foundation Graduate School, University of Minnesota, Rochester,

Bernard Roswit, Chief, Radiotherapy Department, Director, Radioisotope Unit, Veterans Administration Hospital, Bronx, New York

*Moderator* Allan Hurst, Assistant Clinical Professor of Medicine, University of Colorado Medical Center, Denver

**B-4 "Mitral Surgery, Indications and Results"**

Robert P. Glover, Clinical Professor of Thoracic Surgery, Hahnemann Medical College, Instructor in Surgery, Temple University School of Medicine, Philadelphia, David Scherf, Professor of Clinical Medicine, New York Medical College, New York City

*Moderator* Laurence H. Rubenstein, Department of Surgery, Chicago Medical School, Adjunct Thoracic Surgeon, Michael Reese Hospital, Consultant Thoracic Surgeon, Illinois State Hospitals, Chicago

**B-5 "Respiratory Acidosis Recognition and Treatment"**

Bruce Armstrong, Chief, Pulmonary Function Laboratory, Veterans Administration Hospital, Baltimore,

Edwin R. Levine, Assistant Professor of Clinical Medicine, Chicago Medical School, Chicago

*Moderator* Alexander Libow, Associate Attending Physician, Diseases of the Chest, Mt. Sinai Hospital, Miami Beach, Florida

**B-6 "Non-Malignant Esophageal Disease"**

Leon H. Collins, Jr., Associate in Medicine, University of Pennsylvania School of Medicine, Visiting Physician, Philadelphia General Hospital, Philadelphia,

Kenneth A. Wood, Associate Attending Physician, Grace Hospital and Detroit Chest and General Hospital, Detroit

*Moderator* Paul H. Holinger, Professor of Bronchoesophagology, Department of Otolaryngology, University of Illinois College of Medicine, Chicago

**Sunday, June 5****C-1 "Smog"**

Emil Bogen, Clinical Professor of Infectious Diseases, University of California (Los Angeles), Head Pathologist, Olive View Sanatorium, Olive View, California,  
Heinrich Brieger, Professor and Director, Division of Industrial Medicine, Jefferson Medical College, Philadelphia

*Moderator* George Piness, Associate Clinical Professor of Medicine, University of Southern California, Consultant, Long Beach Veterans Administration Hospital, Balboa Sanatorium, Los Angeles

**C-2 "Does a Positive Tuberculin Test Present an Indication for Treatment?"**

Milton I Levine, Associate Professor of Pediatrics, Cornell University Medical College, Associate Attending Pediatrician and Director of the Children's Pulmonary Clinic, New York Hospital, New York City,

James J Waring, Professor Emeritus of Medicine, Colorado University School of Medicine, Denver

*Moderator* Julius Novak, Associate Professor of Medicine, Chicago Medical School, Medical Director, Chicago and Cook County Tuberculosis Institute, Chicago

**C-3 "Cor Pulmonale"**

Arthur C DeGraff, Samuel A Brown Professor of Therapeutics, New York University College of Medicine, Chief, New York University Cardiac Clinic, New York City,

Stephen R Elek, Assistant Clinical Professor of Medicine, University of Southern California, Los Angeles

*Moderator* John H Seabury, Associate Professor of Medicine, Louisiana State University School of Medicine, Director, Lung Station, Charity Hospital of Louisiana, New Orleans

**C-4 "The Place of Surgery in the Treatment of Coronary Artery Disease"**

Edward E Avery, Associate in Surgery, Northwestern University Medical School, Chicago,

Samuel A Thompson, Associate Professor of Surgery, New York Medical College, Director, Thoracic Surgery, Metropolitan Hospital, New York City

*Moderator* John F Briggs, Clinical Associate Professor (Internal Medicine), University of Minnesota Medical School, Minneapolis

**C-5 "Diagnosis and Surgical Treatment of Interatrial Septal Defects"**

Osler Abbott, Assistant Professor of Surgery, Chief, Division of Thoracic Surgery, Emory University Clinic and School of Medicine, Emory University, Georgia,

Henry Swan, Professor of Surgery and Head of the Department, University of Colorado School of Medicine, Denver

*Moderator* Benjamin M Gasul, Clinical Associate Professor of Pediatrics, University of Illinois School of Medicine, Director, Cardio-physiology Department, Cook County Children's Hospital, Chairman, Department of Pediatrics, Presbyterian Hospital, Chicago

**C-6 "What Should we do with Empty Beds in the Tuberculosis Sanatoria?"**

Leonard C Evander, Assistant Medical Director, Niagara Sanatorium, Lockport, New York,

Abel Froman, Tuberculosis Consultant, Manteno State Hospital, Chicago,  
Charles F Taylor, Superintendent and Medical Director, State Sanatorium for Tuberculosis, Norton, Kansas

*Moderator* I D Bobrowitz, Associate Professor of Clinical Medicine (Chest Diseases), Albert Einstein College of Medicine, Visiting Physician (Chest Diseases), Bronx Municipal Hospital Center, New York City

**ADMINISTRATIVE SESSIONS****Wednesday, June 1**

- 8 00 a m Registration (there is no registration fee)  
 2 00 p m Committee on Cancer  
 3 00 p m Meeting, Executive Council

**Thursday, June 2**

- 9 00 a m Joint Meeting, Board of Governors and Board of Regents  
 9 00 a m Committee on Occupational Diseases of the Chest  
 9 00 a m Committee on Resident Fellowships  
 9 00 a m Committee on Scientific Program  
 9 00 a m Sections, Committee on Cardiovascular Disease  
 10 30 a m Committee on College Chapters  
 10 30 a m Board of Examiners  
 10 30 a m Council on Undergraduate Medical Education  
     Committee on Undergraduate Medical Education  
     Committee on Motion Pictures  
     Committee on Audiovisual Aids  
     Committee on College Essay Award  
 10 30 a m Council on Postgraduate Medical Education  
 10 30 a m Council on Public Health  
     Committee on Indian Affairs  
     Committee on Liaison with State and County Medical Societies  
 10 30 a m Committees of the Council on Research  
     Non-Surgical Therapy  
     Pulmonary Surgery  
     Bronchoesophagology  
     Chemotherapy and Antibiotics  
     Physiologic Therapy  
     Bronchial Asthma  
 10 30 a m Committees of the Council on Hospitals  
     Standards and Accreditation  
     Rehabilitation  
     Hospital Statistics  
     Institutions  
     Psychosomatic Aspects  
 12 00 noon **LUNCHEON, 11th ANNUAL COLLEGE CONFERENCE**  
     (Open to all members of the College)  
     William A Hudson, Detroit, Michigan, President, presiding  
     Awarding of Certificates of Merit to Past-Presidents of College Chapters  
     "Our College Chapters"  
     Alvis E. Greer, Houston, Texas, Chairman, Committee on College Chapters  
     "Undergraduate Teaching of Diseases of the Chest"  
     Theodore H Noehren, Buffalo, New York, Vice-Chairman,  
     Council on Undergraduate Medical Education  
 2 00 p m Annual Meeting, Board of Regents  
 2 00 p m Council on Hospitals and Committees  
 4 00 p m **OPEN FORUM, COUNCIL ON HOSPITALS**  
     Charles A Brasher, Mt. Vernon, Missouri, Chairman, presiding  
     Medical Director, Missouri State Sanatorium  
     "Minimum Requirements and Adequate Pay Scales for Sanatorium  
     Personnel"  
     Moderator Edward A Piszczek, Executive Director, Suburban Cook  
     County Tuberculosis Sanitarium District, Hinsdale, Illinois  
     Panel Harold G Curtis, Cleveland, Ohio, Medical Director, Sunny Acres  
     Hospital and Charles W. Scott, Burkeville, Virginia, Medical  
     Director, Piedmont Sanatorium

Discussion from the floor

**ADMINISTRATIVE SESSIONS****Thursday, June 2 continued**

- 4 00 p m Committee on Insurance  
 4 00 p m Council on Undergraduate Medical Education  
           Committee on Undergraduate Medical Education  
           Committee on Motion Pictures  
           Committee on Audiovisual Aids  
           Committee on College Essay Award  
 4 00 p m Council on Postgraduate Medical Education  
 4 00 p m Council on Public Health  
           Committee on Indian Affairs  
           Committee on Liaison with State and County Medical Societies  
 6 00 p m **DINNER MEETING, COUNCIL ON RESEARCH**  
           Open to all members of the College

**Friday, June 3**

- 4 00 p m Editorial Board  
 5 00 p m Committee on College Lectureships  
 5 00 p m Committee on Nominations

**Saturday, June 4**

- 9 00 a m Administrative Session  
           Report of the Historian  
           Report of the Treasurer  
           Report of the Executive Director  
           Report of the Committee on Nominations  
           Election of Officers

**Sunday, June 5**

- 4 00 p m Meeting, Board of Regents  
 6 30 p m Dinner Meeting, Joint Committee on Chest X-Ray

**SOCIAL ACTIVITIES****Saturday, June 4**

- 6 00 p m Annual Convocation (Formal)  
 7 00 p m Cocktail Party (sponsored by The Panray Corp, New York City)  
 7 30 p m Annual Presidents' Banquet  
 9 30 p m Dancing and Entertainment  
           Sponsored by the New Jersey Chapter of the College

**LADIES ACTIVITIES****Thursday, June 2**

- 4 00 p m Tea and Reception, The Shelbourne Hotel

**Friday, June 3**

- 12 00 noon Luncheon, The Ambassador Hotel  
 8 00 p m Theater Party

**Saturday, June 4**

- 6 00 p m Annual Convocation (Formal)  
 7 00 p m Cocktail Party  
 7 30 p m Annual Presidents' Banquet  
 9 30 p m Dancing and Entertainment

**Sunday, June 5**

- 12 00 noon Brunch, The Traymore Hotel

**MOTION PICTURE PROGRAM**

- "Surgical Correction of Aortic Stenosis"  
Charles P. Bailey and Houck E. Bolton, Bailey Thoracic Clinic,  
Philadelphia, Pennsylvania
- "The Use of Shunts in Aortic Arch Disease"  
J. Maxwell Chamberlain, Fort Hamilton Veterans Hospital and Roosevelt Hospital,  
New York City
- "Mechanical Factors Governing Expiratory Obstruction to Airflow"  
Howard G. Dayman, Chronic Disease Research Institute,  
University of Buffalo School of Medicine, Buffalo, New York
- "Treatment of Respiratory Conditions in Children"  
Roy F. Goddard, Pediatrics Research Laboratory,  
The Lovelace Foundation, Albuquerque, New Mexico
- "The Bronchopulmonary Segments Part I Anatomy and Bronchoscopy"  
Chevalier L. Jackson, John F. Huber and Charles M. Norris,  
Temple University School of Medicine, Philadelphia, Pennsylvania (Produced by  
Pfizer Laboratories, Brooklyn, New York)
- "Tetralogy of Fallot"  
John C. Jones, University of Southern California School of Medicine,  
Los Angeles, California (Produced by E. R. Squibb & Sons, New York City)
- "Radical Surgery for Advanced Lung Cancer"  
Adrian Lambert, Columbia University College of Physicians and Surgeons,  
New York City
- "Direct Vision Intracardiac Curative Surgery for Congenital Heart Disease"  
C. Walton Lillehei, R. L. Varco, Morley Cohen and H. E. Warden,  
Department of Surgery, University of Minnesota Medical School, Minneapolis
- "The Genesis of the Electrocardiograph and Intramural Electrocardiography"  
Myron Prinzmetal, Rexford Kennamer, Rashid A. Massumi and Alfred Goldman,  
City of Hope Medical Center and Cedars of Lebanon Hospital,  
Los Angeles, California
- "Gastroesophageal Resection for Carcinoma of the Lower Esophagus"  
Charles B. Puestow, Veterans Administration Hospital, Hines, Illinois
- "Postoperative Aerosol Therapy"  
Max S. Sadove, and Reuben C. Balagot, University of Illinois College of Medicine,  
Chicago (Produced by Winthrop-Stearns, Inc., New York City)

**TECHNICAL EXHIBITORS—21st ANNUAL MEETING**

Air-Shields, Inc.,  
Hatboro, Pennsylvania  
American Cystoscope Makers, Inc.,  
New York, New York  
V. Ray Bennett and Associates,  
Los Angeles, California  
Burnitol Manufacturing Company,  
Boston, Massachusetts  
Warren E. Collins, Inc., Boston,  
Massachusetts  
Joseph K. Dennis Company,  
Chicago, Illinois  
Duncan Oxygen Therapy Company,  
Duncan, Oklahoma  
J. H. Emerson Company,  
Cambridge, Massachusetts  
Ethicon Suture Laboratories,  
New Brunswick, New Jersey  
E. Fougera and Company, Inc.,  
New York, New York  
Grune & Stratton, Inc.,  
New York, New York  
Irwin, Neisler and Company,  
Decatur, Illinois

Eli Lilly and Company,  
Indianapolis, Indiana  
Linde Air Products Company,  
New York, New York  
S. E. Massengill Company,  
Bristol, Tennessee  
Mine Safety Appliances Company,  
Pittsburgh, Pennsylvania  
Mist O<sub>2</sub> Gen. Equipment Company,  
Oakland, California  
National Cylinder Gas Company,  
Chicago, Illinois  
Pacific States Laboratories,  
San Francisco, California  
The Panray Corp.,  
New York, New York  
Chas. Pfizer and Company,  
Brooklyn, New York  
George P. Pilling & Son Company,  
Philadelphia, Pennsylvania  
Sharp & Dohme, Inc.,  
Philadelphia, Pennsylvania  
Smith, Kline & French Laboratories,  
Philadelphia, Pennsylvania

## ADVANCE REGISTRATION FORM

### Urgent Notice

By completing this form and returning it at once to the Executive Offices of the College in Chicago, you will avoid having to stand in line at the Registration Desk in Atlantic City. All of your credentials, as well as luncheon, banquet and other tickets, will be prepared in advance and awaiting your arrival at the hotel. Please complete both sides of this Advance Registration Form and mail promptly. Thank you.

### Please Print

Name

Address

City

State

Accompanied by

Hotel

Arrival date

Departure date

I am enclosing my check in the amount of \$ \_\_\_\_\_ for reservations  
as indicated on the reverse side of this form.

Remarks

Return this form to

Executive Offices  
American College of Chest Physicians  
112 East Chestnut Street  
Chicago 11, Illinois

SEE PAGE XXV FOR HOTEL RESERVATION FORM

*Complete the coupon on reverse side*

TEAR ALONG EDGE

# RESERVATION FORM

## Seminars, Wednesday, June 1

(\$7.50 each)

### MORNING SESSIONS

9 a m - 12 noon

First choice A M

Second choice A M

### AFTERNOON SESSIONS

2 00 - 5 00 p m

First choice P M

Second choice P M

...

*Please indicate choice by number as listed in program*

## Round Table Luncheons

(\$3.50 each)

Friday, June 3

Saturday, June 4

Sunday, June 5

First choice A-

B-

C-

Second choice A-

B-

C-

Third choice A-

B- ..

C-

*Please indicate choice by number as listed in program.*

## Luncheon, 11th Annual College Conference

(\$3.50 each)

Thursday, June 2

I wish to reserve

tickets for the Annual College

Conference, Thursday noon, June 2

## Presidents' Banquet, Saturday, June 4

(\$6.50 each)

I wish to reserve

tickets for the Presidents' Banquet,

Saturday, June 4 (Price includes cocktails, dinner, dancing and entertainment All seats reserved)

*Complete the coupon on reverse side*

**NOTE** Please make checks payable to *American College of Chest Physicians*. Checks must accompany all requests for reservations and will be accepted in the order in which they are received. All tickets will be held for pick-up at the College Registration Desk, Ambassador Hotel, Atlantic City.

# College Chapter News

## ALABAMA CHAPTER

The second annual meeting of the Alabama Chapter will be held in Montgomery, April 20, preceding the meeting of the state medical association, April 21-24. The chapter will present the following program

"Tuberculosis and Pregnancy"

Sydney Jacobs, New Orleans,, Louisiana

Carcinoma of the Lung"

John S LaDue, New York, New York

"Follow-up on Medically Treated Fibro-caseous Nodules"

Raymond F Corpe, Rome,, Georgia

"Broncho-pulmonary Disease with Special Reference to Pulmonary Emphysema"

Herman J Moersch, Rochester, Minnesota

## FLORIDA CHAPTER

The Florida Chapter will hold its seventh annual meeting at the Soreno Hotel, St. Petersburg, April 3, in conjunction with the annual meeting of the state medical association, April 3-6. The following program will be presented

9 00 a m Business Meeting

9 45 a m Scientific Program

"Carcinoma of the Esophagus"

Nelson H Kraeft, Tallahassee

"Changing Laboratory Problems in Tuberculosis"

Albert V Hardy, Jacksonville

"Bronchoplasty in Pulmonary Tuberculosis"

Ivan C Schmidt, West Palm Beach

"Cardiac Contusions"

W Dean Steward and Fred Mathers, Orlando

12 00 noon Luncheon

2 00 p m "Mitral and Aortic Valvuloplasty"

Maurice G Buckles, Columbus, Ohio

"Some Effects of Isoniazid Therapy in Tuberculous Diabetes"

Henry Meyer, Tampa

"Principles of Cardiac Catheterization"

F A Hernandez, Miami

"X-Ray Conference"

(those in attendance are requested to bring x-rays for discussion after presenting a brief and pertinent clinical history)

## OHIO CHAPTER

The Ohio Chapter will meet in Cincinnati, April 20, in conjunction with the annual meeting of the state medical association. The chapter will present the following program

"Experimental Unilateral Pulmonary Artery Occlusion in Man, with Clinical Implications"

Bernard L Brofman, Cleveland

"The Metabolism of Isoniazid"

J Park Biehl, Cincinnati

"The Middle Lobe Syndrome"

Laurence K Groves, Cleveland

"Surgical Significance of Chronic Mediastinal Lymphadenitis"

Charles V Meckstroth



## NEW JERSEY CHAPTER

The New Jersey Chapter will hold a luncheon meeting at the Ambassador Hotel, Atlantic City, April 18. Preceding the luncheon, the chapter will present the following scientific program in conjunction with the Chest Section of the New Jersey State Medical Society

- 10 00 a m "Diaphragmatic Hernia"  
Adrian M. Sabety and Arthur R. Abel, East Orange
- "Indications and Contraindications for Coronary Operations and the Evaluation of Coronary Surgery"  
Nicholas A. Antonius, Newark
- "Surgery of Coronary Heart Disease"  
Alfred R. Henderson, Asbury Park
- "Extent of Thoracoplasty after Pulmonary Resection"  
Philip J. Kundeiman, New Brunswick
- "Atypical Roentgen Configuration of Pleural Effusions"  
Emanuel Klosk and Arthur Bernstein, Newark
- "The Problem of Solitary Circumscribed, Dense, Pulmonary Lesions"  
Samuel Cohen and Frank Bortone, Jersey City
- "Acute Bronchopulmonary Suppuration: Therapy with Endoscopic Application of Oleogenous Penicillin"  
A. Albert Carabelli, Trenton
- "Practical Testing of Pulmonary Function in the Cardio-Respiratory Laboratories of St. Michael's Hospital, Newark"  
Thomas J. Oimsby, Newark
- Motion Picture "Technique of Fluoroscopy of the Chest"  
Paul K. Boinstein, Asbury Park and Irving J. Selikoff, Paterson

## MISSOURI CHAPTER

The annual meeting of the Missouri Chapter will be held jointly with the Missouri Trudeau Society at the Hotel President, Kansas City, March 27, in conjunction with the meeting of the Missouri State Medical Association. The following program will be presented

12 00 noon Luncheon

- 1 00 p m "Recent Advances in Cardiovascular Surgery"  
Hector W. Benoit, Kansas City, Missouri
- "Human Infection with Atypical Acid Fast Organisms"  
(The Yellow Bacillus)
- I "Clinical Manifestations"  
Lawrence E. Wood, Kansas City, Kansas
- II "Pathology and Bacteriology"  
Ann Pollak and Victor Buhler, Kansas City, Missouri
- "The Medical and Surgical Management of Pulmonary Histoplasmosis"  
Medical: Michael L. Furcolow, Kansas City, Kansas  
Surgical: John W. Polk, Mount Vernon, Missouri
- "Report on recent Veterans Administration meetings in Atlanta, Georgia, concerning chemotherapy for tuberculosis"
- Speakers to be announced

## A Brief Discussion of the Etiology of Bronchiogenic Carcinoma

EVARTS A. GRAHAM, M.D., F.C.C.P.

St. Louis, Missouri

It is a high honor which I greatly appreciate to be invited to give the first Jacob Jesse Singer lecture before the American College of Chest Physicians. A close association of approximately 20 years with him gave me the opportunity to recognize his many fine qualities. It was a great shock to me when I received the news that he had been suddenly struck down a few months ago. However, his friends can all be glad that before his death he knew that this lectureship had been established in his honor.

My first acquaintance with him was in the fall of 1919 after my discharge from the army when I went to St. Louis to become the Bixby Professor of Surgery at Washington University. My interest in the future possibilities of chest surgery had been aroused by my connection with the Empyema Commission during World War I. I found Jack to be greatly interested in what we had done and to be particularly well acquainted with the experimental work on pneumothorax which Bell and I had carried out while members of the Commission. He had already begun to specialize in the diagnosis and medical treatment of chest diseases and we naturally fell together as a sort of sympathetic team.

Soon it became evident that it would be desirable for us to have some space in the Barnes Hospital where we could examine patients with a fluoroscope and have daily conferences with each other, with members of the house staff and with such students as cared to attend. We began in some old storage quarters on the second floor which Jack persuaded the superintendent to let us have. We installed a fluoroscope and other equipment and began functioning in the fall of 1920 as a so-called Chest Service. Our conferences became daily occurrences every afternoon—at first for about an hour, and later becoming lengthened to two or three hours. Almost at once we were faced with the problem of an inability to accommodate the number of visitors who wanted to come—not only students and others from our own institutions but from out of town as well.

It was a great personal loss to me when Jack made the decision to go to Los Angeles but fortunately we were able to keep up our friendship.

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From the Department of Surgery, Washington University School of Medicine and Barnes Hospital, St. Louis, Missouri.  
Emeritus Bixby Professor of Surgery, Washington University, St. Louis.  
First Jacob J. Singer Lecture delivered under auspices of American College of Chest Physicians, San Francisco, June 7, 1954.

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by correspondence and by seeing each other at meetings of the American Association for Thoracic Surgery of which he was a long-time and much interested member.

During the days of high mortalities in chest surgery it was a great comfort to me to have Jack's support. At times also he put the brakes on me. The conservatism which he expressed on those occasions, although sometimes resented by me, was probably good for both of us. The younger chest surgeons of today cannot possibly appreciate the criticism both open and veiled which the internists had in the 1920's for those of us who were trying to develop chest surgery. It seemed to be the general opinion of the medical men that to refer a patient to a chest surgeon was the equivalent of notifying St. Peter to expect a new arrival. It required courage for Jack to give me his support during those dark days, for he undoubtedly lost caste among his confieres by doing so. I am glad to make this expression of appreciation even if it is posthumous.

Jack Singer had a gift for things mechanical. Working on his pneumothorax apparatus gave him a great thrill, and when the final model was completed he felt a great satisfaction. It was undoubtedly the most efficient and the simplest to use of any of the apparatuses of the time. His supraglottic aspiration method of using lipiodol for bronchography was a very important addition to our diagnostic armamentarium and unquestionably its invention, by supplanting more cumbersome and even dangerous methods, did much to popularize the use of bronchography.

Now to get to the subject matter of the lecture.

With the exception of a very few die-hards, who refuse to admit the evidence, almost everyone agrees that bronchiogenic cancer, or primary cancer of the lung, has shown a remarkable increase in its incidence during the last 25 years. For example, the vital statistics of the U. S. Public Health Service show that in 1930 the deaths from the condition in men were less than those from cancer of the skin, of the liver, of the rectum, the intestine, the prostate and the stomach. By 1950, however, the most recent year when the statistics are available, bronchiogenic cancer had taken first place in the cancers affecting the male sex, and, from all that is known, the increase is progressing. The incidence of most of the other cancers has shown practically a straight line during the 20 years.

This astonishing increase in the incidence of lung cancer during a short period constitutes a most remarkable phenomenon which apparently is unique in the history of cancer. It behooves everybody, therefore, who is interested in this disease to try to find an explanation.

One other remarkable fact about bronchiogenic carcinoma is that it occurs much more frequently in the male sex. There is a considerable difference in the published statistics of the sexual ratio. Probably about an average ratio would be six males to one female.

Since the rapid increase of this disorder has roughly paralleled the rapid increase in the use of motor vehicles, it was only natural to suspect that perhaps the explanation might lie in the general exposure to some possible carcinogen connected with the automobile. However, in a study of 857 cases of bronchiogenic carcinoma by Wynder and myself (1951) with

special reference to industrial exposures as possible etiological factors, we found no significant increase of this cancer in garage men, automobile mechanics, chauffeurs and oil-field workers. There are, nevertheless, certain other occupations which carry with them increased risks of developing the condition. Probably the most striking examples were brought out in the well-known studies made on the Schneeberg and Joachimsthal miners with incidences of 40 per cent and 48 per cent respectively of deaths from lung cancer in the two places. The interested reader may find an excellent review of the occurrence of the disorder among those miners in the article by Lorenz (1944). More recently the chromate industry has been found to be associated with a higher incidence of lung cancer than the general population. This association has been well described by Mancuso and Hueper (1951). However, one can hardly blame such industrial associations for the tremendous increase in incidence of the disease because of the relative insignificance of the numbers engaged in those industries. Kotin has recently discovered some carcinogens in the atmospheric smog of Los Angeles. But it would be difficult to incriminate atmospheric pollution for the widespread increase of bronchiogenic carcinoma because if that were a responsible factor women undoubtedly would be victims of the disease as often as men. Moreover, as Peacock of Glasgow has informed me, there are analyses of the atmosphere of that city which were made a century ago that show practically the same composition as today. It would seem therefore that if atmospheric pollution is an important etio-

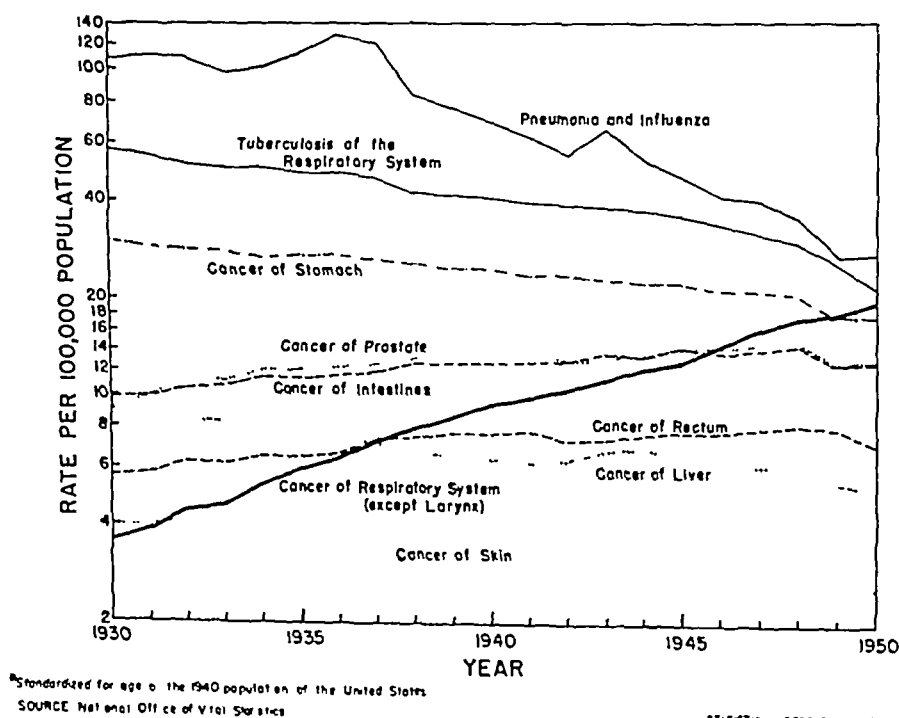


FIGURE 1 Death rates for selected respiratory diseases and sites of cancer among white males, United States 1930-50 (Rates standardized for age on the 1940 population) The chart shows the rapid rise in the curve of incidence of cancer of the respiratory system in comparison with the nearly straight lines of other common cancers (Prepared by Dr. E. Cuyler Hammond, chief statistician of American Cancer Society, and reproduced with his permission.)

logic factor there would not have occurred the same recent great increase in the incidence of lung cancer in Glasgow that has been noted elsewhere in Great Britain and in the United States

Another possible etiologic factor that has been suggested frequently is tobacco smoking. This suggestion was made as long ago as 1912 by Adler who wrote the first monograph on primary lung cancer at a time when the condition was still rare. Brosch in 1900 had made some unsuccessful attempts to produce cancer experimentally in guinea pigs by painting them with tobacco "juice." The list of additional writers who since then have mentioned smoking as a possible factor is a long one. Most of them, however, were content to make the suggestion and did nothing further to find out. However, a few submitted their idea to experimental studies, but the experiments were not conducted for a long enough time and in some instances the method of study is not reported in sufficient detail to make the results satisfactory. For example, Hoffmann and his associates painted their animals (mice) for only 14 days, a very inadequate length of time, but they did observe hair loss. Wacker and Schmincke noted epithelial proliferation in rabbits' ears 21 days after a subcutaneous injection of pipe tar. Lorenz and his co-workers failed to obtain pulmonary

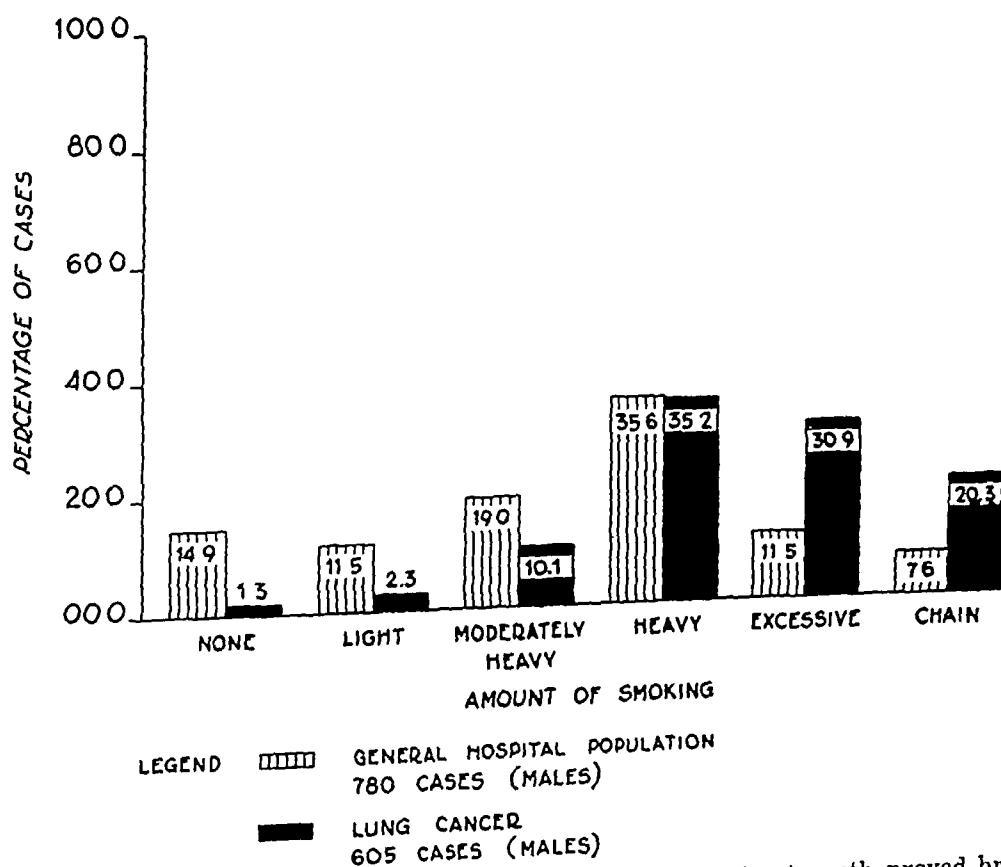


FIGURE 2 The amount of cigarette-smoking in 605 male patients with proved bronchiogenic carcinoma as compared with 780 males over 35 years of age without cancer of the lung (Wynder and Graham 1950). The arbitrary classifications of smoking are as follows: Non-smokers (less than one cigarette per day for more than 20 years), light smokers (up to one-half pack per day for more than 20 years), moderately heavy (one-half to three-quarters of a pack), heavy smokers (three quarters to a whole pack), excessive smokers (one to one and three quarters packs), chain smokers (more than one and three quarters packs).

tumors in mice which were made to inhale tobacco smoke. The literature on the attempts to produce cancer experimentally has been summarized in an article by Wynder, Graham and Croninger (1954). Ochsner and DeBakey in 1941 called attention to the similarity of the curve of the increased sales of cigarettes in this country to the greater prevalence of primary cancer of the lungs and concluded from those curves that there is a possible etiologic relationship between cigarette smoking and bronchiogenic carcinoma.

In spite of sporadic suggestions of an etiologic relationship and a few experimental attempts to produce cancer with tobacco products no large scale study was undertaken to try to determine such a possibility until 1949 when Wynder and the writer began theirs. In May, 1950, that study was published. It was based on 684 proved cases of bronchiogenic carcinoma. Nearly all the patients were in the Barnes Hospital, St. Louis, but the sampling was not restricted to a small locale since the patients came from many places in the Middle West and Southwest of the United States. They were interviewed about their smoking habits by one of two non-medical young women who used a standard questionnaire which had been devised by us. The study brought out the fact that of 605 men with bronchiogenic carcinoma, other than adenocarcinoma, no less than 86.5 per cent had smoked from about a pack to more than two packs of cigarettes a day for at least 20 years, and among those men with the two com-

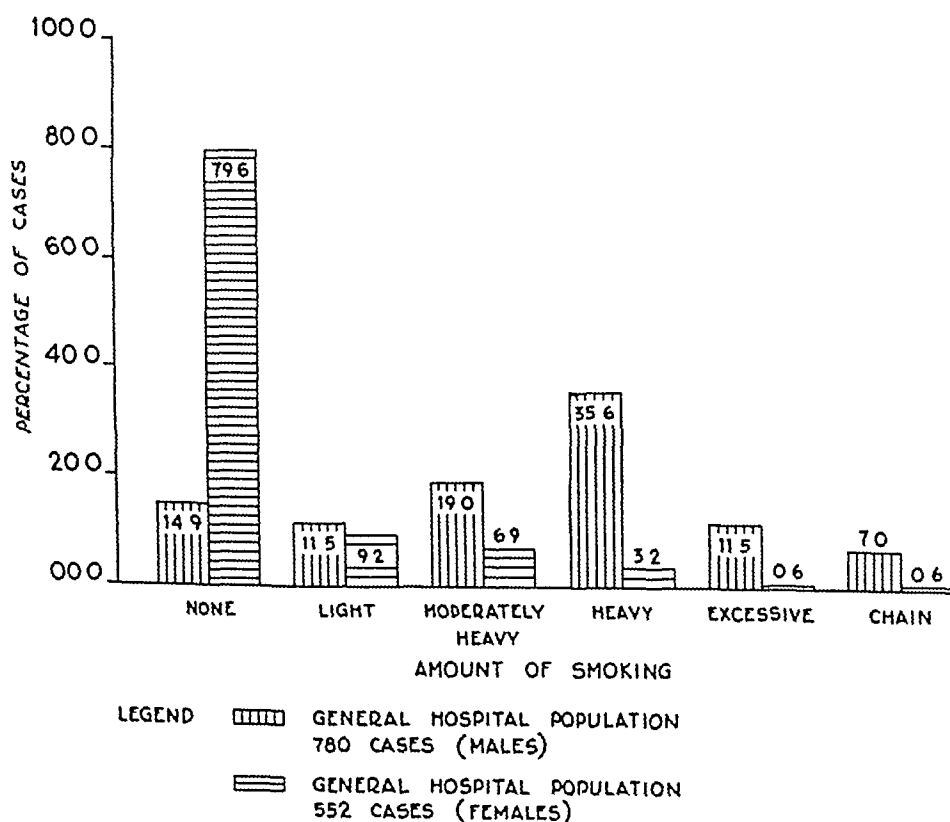


FIGURE 3 This chart shows to be false the common idea that women smoke as much as men. The statistics were obtained by questioning 780 male and 552 female patients in the Barnes Hospital. None of the patients had a bronchial carcinoma and all were more than 35 years old.

mon types of carcinoma (epidermoid and undifferentiated) only 13 per cent were non-smokers. Of a control group of 780 men without lung cancer 54.7 per cent had a similar history of heavy smoking of cigarettes but as many as 14.9 per cent were non-smokers. Another important finding was that no less than 72 per cent of the lung cancer patients stated that they had smoked from 30 to 50 years. Our study also showed to be erroneous the current opinion that women smoke as much as or more than men. Of 552 women patients without lung cancer and above the age of 35, in the Barnes Hospital, no less than 79.6 per cent of them were non-smokers, as compared with only 14.9 per cent of men in a similar group. It is the young women and the girls, rather than the women of the cancer age, who do the heavy smoking. Moreover, they are too young to have smoked the necessary time to develop a lung cancer, 25 years or so.

Our results were strikingly confirmed by the publication in September, 1950, of the now well-known statistical study of Doll and Hill in England. Their study was being made at the same time as ours, but we happened to precede them in publication by a few months. It was based on about the same number of patients as ours. Of 649 men with lung cancer they found only 0.3 per cent of non-smokers, compared with our figure of 1.3 per cent. As in our series Doll and Hill found that a high percentage of the men with cancer were heavy cigarette smokers. They concluded that their findings "suggest that, above the age of 45, the risk of developing the disease increases in simple proportion with the amount smoked, and that it may be approximately 50 times as great among those who smoke 25 or more cigarettes a day as among non-smokers."

In addition to our own and that of Doll and Hill there have been 10 other statistical studies reported, making 12 in all (Dungel 1950, Levin et al 1950, Mills and Porter 1950, Schrek et al 1950, Gsell 1951, McConnell et al 1952, Kouloumies 1953, Sadowsky et al 1953, Wynder and Cornfield 1953 and Bieslow et al 1954). The results of all of the 12 studies have been essentially the same. They have all shown that cancer of the lung occurs nearly always in heavy cigarette smokers. It is very significant that no study has been reported which gives any different conclusion. The skeptics should ponder that fact.

The general agreement among all the statistical studies is very strong evidence in itself that there is a definite etiologic relationship between excessive cigarette smoking and cancer of the lung. Yet obviously that relationship would seem to be more definitely established if cancer could be produced experimentally by the use of cigarette smoke. Earlier in this article brief mention has been made of a few of the experimental attempts using various tobacco products. The literature pertaining to this earlier work has been summarized in an article by Wynder, Cioninger and myself published in 1953. For the most part the results have been negative, although a total of seven epidermoid cancers of the skin have been reported as having been obtained in mice with products of cigarette smoke out of many animals used. Most workers who have attempted to cause experimental cancer with tobacco products have used rabbits. Roffo (1939) reported the successful production of carcinoma in rabbit ears after paint-

ing them with a distillate of tobacco, but Sugiura failed in his attempt to reproduce Roffo's results. Also Flory (1941) succeeded in obtaining only what he called "carcinomatoids" in rabbit ears after application of a tobacco distillate.

It seemed therefore that the actual experimental production of carcinoma by the use of tobacco products had been so rare that a doubt could be raised that in any instance an etiologic relationship had been established. On the basis of that conclusion we decided to undertake some experiments to determine if cancer could be produced by the use of tar from cigarette smoke. It seemed to us highly desirable, if possible, to bring some experimental evidence to this controversial subject, in addition to the statistical evidence. An especially important point was to use a proper strain of mice which is known not to develop spontaneous cancers of the skin. In the study therefore we used the inbred strain known as CAF<sub>1</sub> that was developed in Dr. C. C. Little's laboratory at Bar Harbor, Maine, and that is known to be free from spontaneous tumors of the skin.

A machine was devised by which, with a small electric motor, we smoked 60 cigarettes at a time. The smoke was collected in flasks cooled by dry ice. The sudden chilling of the smoke precipitated the tar from it which was dissolved in acetone. The acetone solution was painted on the skin of the mice\* three times a week, after it had been evaporated to a composition of equal parts of tar and acetone. Control mice painted with acetone alone showed no reaction of the skin whatever—not even any evidence of irritation.

Papillomas appeared in 59 per cent (26 females and 22 males) of 81 tarred CAF<sub>1</sub> mice. Although 8.6 per cent of the papillomas regressed, no less than 44.4 per cent (or 36 mice) developed epidermoid cancer of the skin. Sometimes there were two cancers in one mouse and in one case there were three, but in most instances only one cancer appeared in the painted area. In view of the much greater frequency of bronchiogenic carcinoma in the human male it was of special interest that among the tarred mice 25 of the cancers appeared in females and only 11 in males.

Successful transplantation of the experimentally produced cancers into normal mice was easily accomplished, and in one instance a transplantation has been carried out through more than 30 generations. Of course the importance of the successful transplantations is the positive evidence of malignancy of the growth which they demonstrate.

An observation of importance that we made in connection with the experiments was that the average time of appearance of a cancer was after 71 weeks of painting. This period of time represents a little more than one-half the average life-span of the mouse, which is ordinarily a little more than two years. This time corresponds roughly with the period of smoking required for the production of a bronchiogenic cancer in the human. For our statistical observations demonstrated that 30 to 50 years of smoking precede the appearance of a bronchiogenic carcinoma, a period roughly corresponding to one-half the life span.

\*For details of the experimental work our original article (Wynder, Graham and Croninger, 1953) should be consulted.



Our experiments demonstrate beyond a possibility of doubt that cigarette smoke contains something which is carcinogenic for the skin of mice

Is this finding of significance in relation to the question of human bronchiogenic carcinoma?

It would seem to the writer that, even when taken alone, the finding of a carcinogenic substance in cigarette smoke is of very great significance. When combined with the findings of the statistical studies the importance



FIG 4

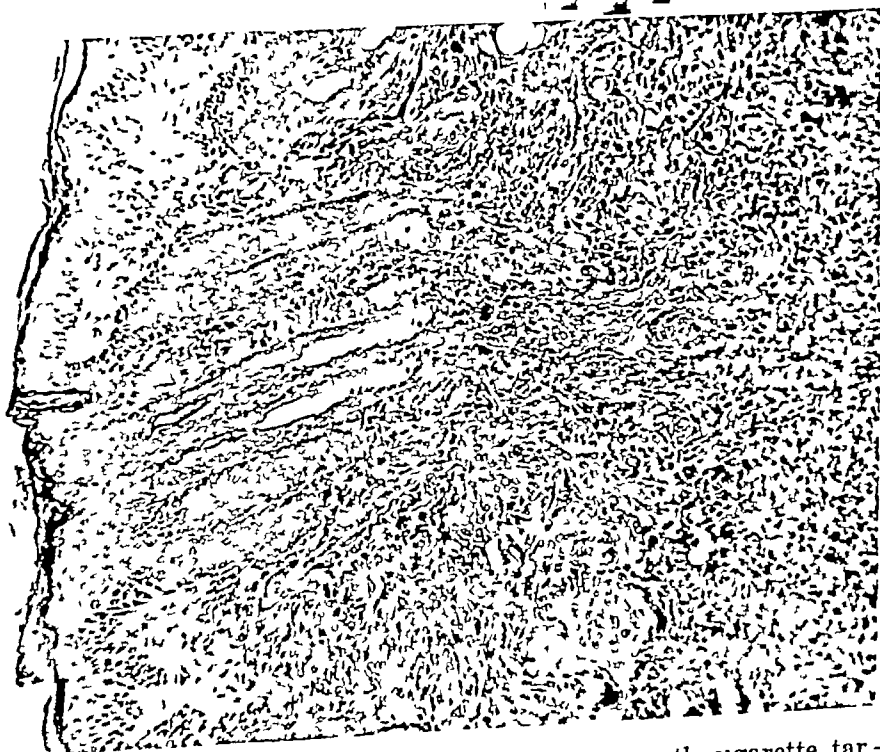


FIG 5

Figure 4 Beginning carcinoma after 322 days of painting with cigarette tar —  
Figure 5 Photomicrograph of same lesion at 371 days

of these experimental observations is greatly increased. To many the fact that all the published statistical studies point in the same direction together with now the successful production of epidermoid cancer in mice by painting the skin with the tar derived from cigarette smoke makes the chain of evidence incontrovertible. Others, however—and these are usually heavy cigarette smokers—decry the significance of our experimental results. They state that no absolute proof has been produced that there is any etiologic relationship between cigarette smoking and cancer of the lung.

It must be admitted that the proof of a definite relationship does not exist. To establish such proof to the satisfaction of the “die-hards” would require human experimentation carried out on the same individuals for more than a quarter of a century. Obviously such experiments cannot be conducted. Perhaps one could say that if the agent involved in the case were something less desired by the users of it than are cigarettes by their habitués there would be no difficulty in the general acceptance of the evidence. If, for example, the findings pointed to a substance like spinach as the guilty party instead of the habit-forming cigarette, would there be as much difficulty in accepting the evidence?

By many of the writers on this subject there is too much of a tendency to consider bronchiogenic carcinoma as if it were one disease. On the contrary there is much evidence to indicate that there are several varieties which are so different from each other that probably they represent actually different diseases. At least three varieties can be easily distinguished with different etiologies. The fact that smoking is not a causative factor in at least two of the three varieties leads to confusion in the minds of some observers who are not aware of the differences because, as they state, they can cite cases in which the patients never smoked.

The three varieties which seem to me to be clearly distinguishable from each other are

- (1) The epidermoid or squamous cell. Sometimes the structure of this tumor is not clearly differentiated, and for that reason I like to include in this group the so-called “undifferentiated” cancers. This group is the common bronchiogenic carcinoma which in our experience constitutes well over 90 per cent of all bronchial cancers. At the present time it occurs much more commonly in the male. It is found very rarely in a non-smoker. It is this variety of lung cancer which has shown the very striking increase in incidence.

- (2) The adenocarcinoma. When typical this tumor has several characteristics which set it apart from the epidermoid cancer. For one thing, our statistical studies showed that it has a much less close relationship to smoking. In our series, out of 39 men with adenocarcinoma no fewer than four (10 per cent) were non-smokers, whereas among the other 605 men with bronchiogenic carcinoma the proportion of non-smokers was only 1.3 per cent. Even more remarkable was the fact that of 15 women with adenocarcinoma 13 were non-smokers. Another characteristic of the adenocarcinoma which distinguishes it from the epidermoid variety is that it occurs with about equal frequency in the two sexes. Again, the adenocarcinoma has a special tendency to involve younger people, or, to put it

in another way, whenever a young person has a bronchiogenic carcinoma it is nearly always an adenocarcinoma Olson (1935) states of 576 cases of lung cancer compiled from the literature by Brunn in 1926, 12 per cent were in the age group 20-29, and all of them were adenocarcinoma These characteristics seem to set off this tumor from the more common epidermoid cancer and to suggest that it is a different disease entity with a different etiology Perhaps in at least some cases the adenocarcinoma has had



FIG 6



FIG 7

Figure 6 Advanced carcinoma (2 lesions) in another mouse at 590 rays of painting —  
Figure 7 Photomicrograph of lesion at left.

its origin in a so-called bronchial adenoma which has become malignant. In 1938 Womack and I presented evidence that the so-called bronchial adenoma is a potentially malignant tumor capable of producing both regional and distant metastases. Such an idea at that time was not generally accepted but there are few who oppose it now. A common microscopic pattern seen when the tumor has become malignant is that of an adenocarcinoma. It would seem reasonable to conclude therefore that at least some of the adenocarcinomas have arisen in bronchial adenomas.

(3) The so-called alveolar-cell carcinoma. This type is rare compared with the other two types. Both the gross appearance of the involved lung and the microscopic characteristics of the tumor resemble very closely the disease of sheep known by the South African word, "jagziekte." It is probably due to a virus.

[Note: Some of the text and illustrations appearing in this article were previously published in my Sir John Fraser Lecture, delivered at the University of Edinburgh, May 11, 1954, and printed in *Lancet* of June 26, 1954, pp 1305-1308. This material is reproduced here with the permission of the editor of *Lancet*.]

### CONCLUSIONS

(1) A very remarkable increase in the incidence of bronchiogenic carcinoma has occurred in the last 25 years. From having been a curiosity in 1930, by 1950 it was so common that it had become the most frequent cancer in the male sex.

(2) No less than 12 statistical studies have shown a definite etiologic relationship between the disease and excessive cigarette smoking. Of equal importance, perhaps, is the fact that no careful study has been published which fails to show that relationship.

(3) The statistical evidence has been strongly supported by the experimental production of epidermoid carcinoma in the skin of CAF<sub>1</sub> mice by painting the skin with tar obtained from cigarette smoke. The incidence of cancer production was 44.4 per cent in 81 tarred mice.

(4) A mistake is commonly made in thinking that bronchiogenic carcinoma is a single disease. Actually there seem to be at least three separate varieties with different etiologies.

### RESUMEN

1 En los últimos 25 años ha habido un notable aumento en la frecuencia del carcinoma bronquigénico. Siendo una curiosidad en 1930, ya en 1950 es tan común que se ha convertido en el cáncer más frecuente en el sexo masculino.

2 No menos de doce estudios estadísticos han demostrado de finidamente una relación etiológica entre la enfermedad y el fumar excesivo. De igual importancia quizás, es el hecho de que no se ha ya publicado un estudio cuidadoso que deje de mostrar esa relación.

3 La evidencia estadística es soportada fuertemente por la producción experimental del carcinoma epidermoide de la piel de los ratones CAF por medio de las embrocaciones de la piel con el alquitrán obtenido del humo de cigarrillos. La incidencia de la producción del cáncer fué de 44.4 por ciento en 81 ratones alquitrados.

4 Es un error común el considerar que el carcinoma bronquiogénico es una sola enfermedad. De hecho parece que hay cuando menos tres diversas variedades con etiologías diversas

### RESUME

1 Dans les 25 dernières années, on a noté une augmentation très importante de la fréquence du cancer bronchique. Considéré comme une curiosité en 1930 il était si répandu en 1950 qu'on pouvait le considérer comme le cancer le plus fréquent dans le sexe masculin.

2 Douze études statistiques au moins ont montré une relation étiologique incontestable entre cette affection et la consommation excessive de cigarettes. Peut-être faut-il attacher la même importance au fait qu'aucune étude attentive n'a été publiée concernant les cas où cette relation n'a pu être mise en évidence.

3 Les constatations statistiques ont été renforcées solidement par la production de cancers épidermoïdes sur la peau de souris après application de goudron extrait de la fumée de cigarette. Sur 81 souris ainsi préparées, il y eut 44,4% de cancer.

4 C'est une erreur commune de penser que le cancer bronchique est une maladie simple. Actuellement, il semble qu'il y a au moins trois variétés différentes de cancer avec des étiologies diverses.

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# Is Survey Cancer of the Lung Curable?

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Lung cancer has increased precipitously in the last 30 years. The increase can probably be estimated by the trend in death rates, so closely does morbidity approach mortality. While a few thoracic surgeons are sanguine about their results, the over-all five year survival rates continue to be under 10 per cent. Is this disease curable—or would it be if we could detect it earlier? By what means is early detection possible? Some authors suggest that chest x-ray surveys are an answer.<sup>1,2,3,4</sup>

Since the official Philadelphia Chest Survey Program has been as interested in detecting lung cancer as in finding active tuberculosis, it seems appropriate to examine the survival rates of survey cancer patients. In 1949, through following survey cases suspected of having tuberculosis, it became evident that lung cancer was masquerading as tuberculosis. Therefore, policy was inaugurated for reporting as "Suspect Neoplasm" all abnormalities for which this seemed a possible diagnosis. Liaison with hospitals is excellent so that diagnostic studies may be promptly obtained. In addition, there is meticulous follow-up of all persons with abnormal photofluorograms. The fate of primary bronchogenic carcinoma cases detected at these units may help illuminate the role of surveys in finding curable lung cancer.

## *Materials and Methods*

The prevalence of persons classified as "Suspect Neoplasm" was examined because the promptness of resection is related to the index of suspicion.

The prevalence of proved cancer cases was studied by age, race, and sex among 142,156 persons on whom appropriate basic data were available. Sixty-three per cent of these persons were foodhandlers required by law to have annual chest roentgenograms.

A list was made of 100 consecutive carcinoma cases detected at two official Philadelphia City Chest X-ray Units beginning with January, 1947. Only those were included whose diagnoses were confirmed pathologically by tissue obtained at operation, by biopsy and by autopsy. In eight instances in which the clinical course and roentgenographic changes on serial films were consistent, positive cytologic reports on bronchial secretions were accepted as proof.

Resectability and survival rates were studied and correlated with age, race, sex, photofluorographic appearance, presence or absence of symptoms at the time of the first photofluorogram recognized as abnormal, broncho-

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scopic appearance, bronchoscopic biopsy, cytologic reports on bronchial secretions and tissue diagnoses

Detailed survival studies were limited to three-year survival rates on 57 persons whose first abnormal photofluorograms had been taken at least three years before the close of the study

Concomitant tuberculosis was studied. Only those cases were accepted as active tuberculosis in whom the clinical diagnosis was substantiated by more than one positive sputum. In two instances the coexistence of tuberculosis was found by post mortem examination

Patients were divided into two categories—58 “preclinical” who had not sought medical advice prior to the time of the first recognized abnormal photofluorogram and 42 “clinically manifest” who had consulted physicians because of respiratory symptoms. The “preclinical” patients were further subdivided into 10 who were truly asymptomatic and 48 who, on careful questioning, were found to have respiratory symptoms

A study was made of the interval between the first abnormal photofluorogram and the hospitalization resulting in the diagnosis of carcinoma. When hospitalization had been effected within one week, it was considered there had been no delay. The total delay period was broken down according to the following components: delay attributable to (1) radiologist, (2) administration, (3) clinician, (4) patient, and (5) difficulty in obtaining hospital beds.

Radiological delay was limited to those delays which had deferred referral to a clinician. If the photofluorographic reading had been such that the patient had been expeditiously referred even though the radiologist had not suspected neoplasm, delay was not attributed to the radiologist since surveys are screening processes, not diagnostic in nature. It seemed fair to assume that, if a patient was hurried to a clinician because of an abnormal film, it was the clinician's responsibility to proceed as rapidly as possible to the definitive diagnosis

In 29 instances, earlier photofluorograms were available for retrospective review

In connection with the 81 deaths, the median interval was studied between the abnormal photofluorogram and death for the various factors suspected of having prognostic significance

Follow-up was closed as of August 31, 1953, yielding data on a period of three to 80 months

## RESULTS

### *Prevalence of Photofluorograms Suggesting Neoplasm*

As follow-up experience was correlated with photofluorographic readings, the rate per 100,000 of photofluorograms read as “suspect neoplasm” increased from 135 in 1949 to 219 in 1953. The rate for men over 45 was 556. Guiss<sup>3</sup> reported that 190/100,000 photofluorograms were interpreted as suggesting neoplasm in the 1950 Los Angeles Survey in which 1,867,201 persons were x-rayed

Of 607 persons at all ages whose photofluorograms were interpreted as “suspect neoplasm,” 10 per cent were proved to have bronchogenic carci-

noma Of the men over 45 years of age with such readings, 18 per cent had lung cancer

Prevalence rates of proved primary cancer per 100,000 persons surveyed were 37 for the whole group of 142,156, three for females, and 69 for males For males over 45, the rate was 284 (Table I) (Figure 1) There was no significant difference between whites and non-whites The prevalence of proved lung cancer in the Boston survey was only 7/100,000<sup>5</sup> This low prevalence is not due to basic differences between the Boston and Philadelphia surveyed populations since the Philadelphia group was younger and had fewer males over 45 than had the Boston group

### *Resectability*

Resectability is essential to survival However, it is not an end in itself The anguish and expense of surgery are only meaningful when cures are obtained Therefore, resectability rates are of interest but the vital figures are on those resected who have survived for significant periods of time

Of the 100 cases, 52 were explored but only 30 were resected, a rate slightly below that reported by Gibbon et al<sup>6</sup> and McDonald<sup>7</sup> but higher

TABLE I  
PREVALENCE OF PROVED BRONCHOGENIC CARCINOMA  
AMONG INDIVIDUALS REFERRED TO  
TWO OFFICIAL PHILADELPHIA UNITS\*  
BY AGE, RACE AND SEX

Under 45	Number	Subtotals	Proved Bron Ca	Subtotal Bron Ca	Rate / 100 000
Male White	26,916		1		4
Male Non-White	29,200		2		7
All Males Under 45		56,116		3	5
Female White	30,495		1		3
Female Non-White	28,110		—		—
All Females Under 45		58,605		1	2
Over-all Total Under 45	114,721		4		3
Over 45	Number	Subtotals	Proved Bron Ca	Subtotal Bron Ca	Rate / 100 000
Male White	12,076		27		224
Male Non-White	4,501		20		444
All Males Over 45		16,577		47	284
Female White	7,809		1		13
Female Non-White	3,049		—		—
All Females Over 45		10,858		1	9
Over-all Total Over 45	27,435		48		175
Over-all Total	142,156	142,156	52	52	37
Total Males	72,693		50		69
Total Females	69,463		2		3

<sup>5</sup>Unit 1—Total 1947, foodhandlers only 1949 through 1952

Unit 3—Total 1949 through 1952



# PREVALENCE RATES/100,000 OF PROVED BRONCHOGENIC CARCINOMA AMONG PERSONS SURVEYED AT 2 OFFICIAL PHILA UNITS\*

FEMALES  
69,463 ☐ 3

TOTAL  
142,156 ☐ 37

MALES  
72,693 ☐ 69

MALES  
OVER 45 ☐ 284  
16,577

\* UNIT 1 - TOTAL 1947, FOODHANDLERS ONLY 1949 THRU 1952

UNIT 3 - TOTAL 1949 THRU 1952

FIGURE 1

than that reported by most thoracic surgeons. When it is considered that the 52 explorations were undertaken at 18 different hospitals, the resectability rate of 30 per cent seems quite good.

Nothing striking was found in correlating resectability with age, race, sex, photofluorographic classification or clinical status. However, as in all reported series, there was a higher resectability for those with squamous cell carcinoma (Table II).

TABLE II  
RESECTABILITY ACCORDING TO TISSUE DIAGNOSIS

Tissue Diagnosis	Number	Number Resected	Per Cent Resected
Squamous	59	22	37
Adenocarcinoma	16	4	25
Undifferentiated	19	4	21
Unclassified	6	—	—
Total	100	30	30

Fifteen patients were never bronchoscoped. Their diagnoses were made by autopsy in 12 and by biopsy in three instances. Reports are not yet available on two patients. Twice as high a percentage of the 21 patients with grossly normal bronchoscopic findings were resected as of the 62 with any abnormal findings at all (Table III). The gross bronchoscopic findings were as follows:

## GROSS FINDINGS ON 81 CANCER CASES\*

Normal	21	Stenosis	2
Tumors visualized	27	Bloody Secretion	8
Compression or Distortion	20	Mucosal Thickening	3**
		Excessive Secretions	4

\*Categories not mutually exclusive

\*\*Biopsies positive

Twenty-one had positive cytologic reports. A third of these were resected. One-fifth of the 28 with positive bronchoscopic biopsies were resected (Table III).

TABLE III  
RESECTABILITY ACCORDING TO BRONCHOSCOPIC FINDINGS

	Number	Number Resected	Per Cent Resected
Not Bronchoscope	15	—	—
Bronchoscope*	85	30	35
Total	100	30	30
<i>Gross Bronchoscopic Findings</i>			
Normal	21	12	57
Abnormal	62	18	29
<i>Microscopic Findings**</i>			
Positive Cytology	21	7	33
Positive Biopsy	28	6	21

\*Reports not available on 2

\*\*Categories not mutually exclusive

### Over-all Survival

There are 19 survivors out of the group of 100. Fourteen of the survivors have been resected. Because of the variable length of follow-up, survival was studied by the life table method (Tables IV, V, and VI) as well as by direct observation (Figure 2). Survival rates were very close to each other by both methods.

Half the patients with survey-detected lung cancer died within the first year of their abnormal films (Table IV) (Figure 2). In our experience the chance of a survey-detected case being resected and living five years is about 10 per cent (Table V). We do not believe it is sound to dwell on the figures restricted to resected cases only. The opportunity for resection is too rare.

TABLE IV  
SURVIVAL OF PROVED CASES OF BRONCHOGENIC CARCINOMA  
BY YEARS AFTER ABNORMAL PHOTOFLUOROGRAM\*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent
0-1	100	49	8	49	100
1-2	43	16	2	62	49
2-3	25	10	4	57	30
3-4	11	3	1	71	17
4-5	7	3	—	57	12
5-6	4	—	4	—	**

\*Computed by the Life Table Method using the equation  $n \lambda = \frac{d}{n \lambda}$

\*\*Numbers too small for percentage estimation

$$\frac{O - W}{x} \times \frac{x}{2}$$

# SURVIVAL ACCORDING TO LENGTH OF FOLLOW-UP.

## 90 CASES WITH MINIMAL 1 YR. F. U.

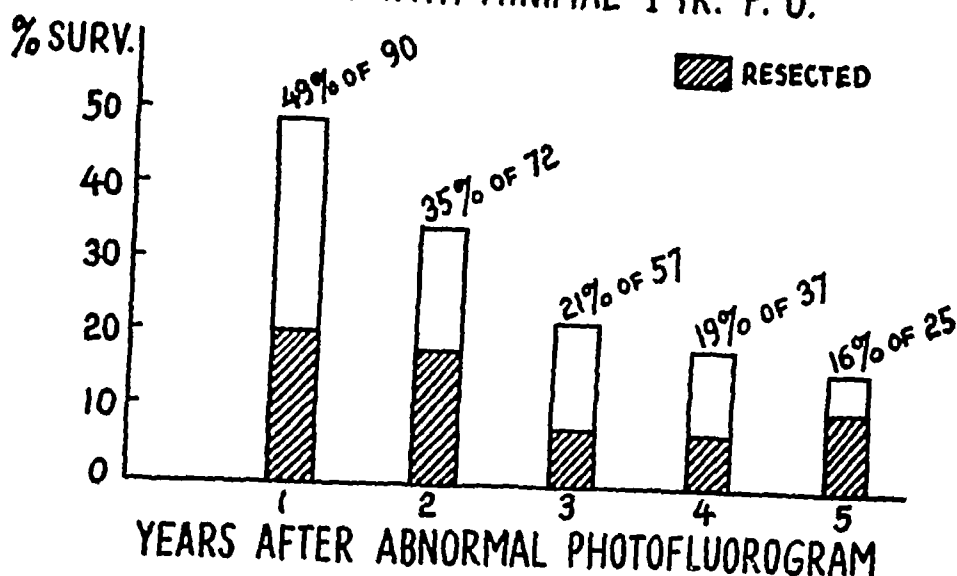


FIGURE 2

Hospital mortality was 17 per cent for the 52 thoracotomies. Five (23 per cent) died of the 22 explored but not resected and four (13 per cent) died of the 30 resected. Of the 26 who survived resection, nine died within the first postoperative year. The longest interval between the abnormal photofluorogram and death in an unresected case has been five years, one month.

Of the 57 persons on whom three-year survival rates could be calculated, 12 (21 per cent) survived three years. Only five of these have been resected, so that ultimate survival cannot be better than the dismal figure of nine per cent. The three-year survival rate for the 39 Boston cases is 13 per cent<sup>5</sup>. Where the prognosis is so poor, it is difficult to decide what factors are related to prognosis. The following factors were studied in an attempt to find some guides for case-finding efforts.

TABLE V  
SURVIVAL OF RESECTED CASES IN YEARS AFTER  
FIRST ABNORMAL PHOTOFLUOROGRAM\*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent	Proportion Resected and Alive <sup>1</sup>
0-1	30	6	7	77	100	30
1-2	17	5	—	71	77	23
2-3	12	4	4	60	55	16
3-4	4	1	—	**	33	9.6
4-5	3	—	—	**	**	**
5-6	3	—	3	**	—	—

\*Computed by the Life Table Method using the equation 
$$n_x = \frac{d}{\frac{n \lambda}{O - W} \times \frac{x}{2}}$$

\*\*Numbers too small for percentage estimation

*Survival According to Age, Race and Sex*

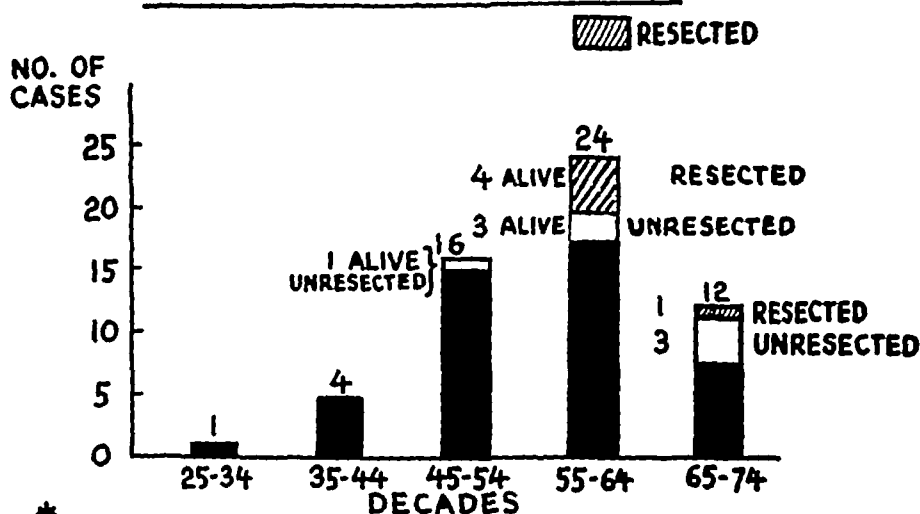
Bronchogenic carcinoma may be more malignant in younger persons. Of the 21 younger than 55 on whom three-year survival studies could be

TABLE VI  
SURVIVAL OF UNRESECTED CASES IN YEARS AFTER  
FIRST ABNORMAL PHOTOFLUOROGRAM\*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent	Proportion Resected and Alive <sup>1</sup>
0-1	70	43	1	32	100	70
1-2	26	11	2	56	32	22
2-3	13	6	—	54	18	12
3-4	7	2	1	69	10	6
4-5	4	3	—	**	7	4
5-6	1	—	1	**	**	**

\*Computed by the Life Table Method using the equation 
$$n \lambda = \frac{d}{\frac{O - W}{\frac{x}{2}}}$$

\*\*Numbers too small for percentage estimation

**SURVIVAL ACCORDING TO AGE\***

\*LIMITED TO 57 PATIENTS WITH MINIMAL 3 YEAR FOLLOW-UP.

FIGURE 3

TABLE VII  
SURVIVAL ACCORDING TO AGE

Age Groups Years	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
30-34	1	—	—	—	—
35-44	4	—	—	—	—
45-54	16	1	6	—	—
55-64	24	7	29	4	17
65-74	12	4	33	1	8
Total	57	12	21	5	9

calculated, only one survived three years and she died shortly thereafter (Table VII) (Figure 3). The poorer prognosis of younger persons was not due to a low index of suspicion because, among the 57 with a minimal three-year follow-up, the median delay in hospitalization was  $2\frac{1}{2}$  months less (207 days) for those under 55 than for those over 55 (283 days)

Another indication that lung cancer may be more malignant for younger persons is the shorter median survival time for those who died. In the over-all series, the figures were six months for the deaths in those younger than 45 compared with 10 months for those 65 to 74 (Figure 4)

There was no significant difference in survival between whites and non-whites

#### *Survival According to Photofluorographic Appearance*

The three-year survival rate of those whose films were interpreted as "Tuberculosis" was 24 per cent (Table VIII) in contrast to the rate of 33 per cent for the "erroneous negatives"

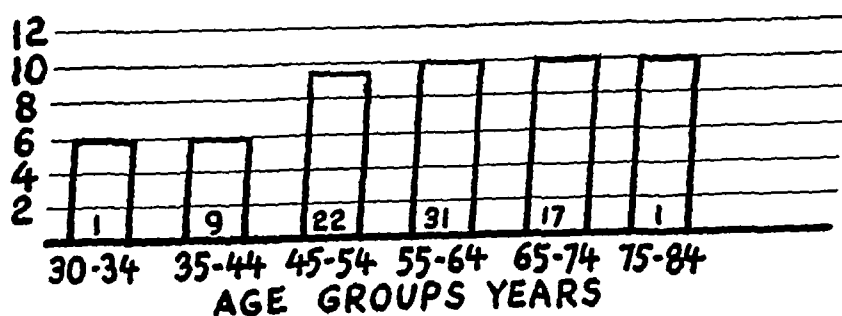
TABLE VIII  
THREE YEAR SURVIVAL ACCORDING TO  
PHOTOFLUOROGRAPHIC APPEARANCE

Photo- fluorographic Classification	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Suspect Neoplasm	21	2	10	1	5
Tuberculosis Only	17	4*	24	1	6
Suspect	4	1	**	1	**
Erroneous Negative	15	5	33	2	13
Total	57	12	21	5	9

\*Three of these 4 died within the next 2 years. The sole survivor is unresected  
\*\*Numbers too small for percentage estimation

### MEDIAN SURVIVAL BETWEEN ABNORMAL PHOTOFLUOROGRAM AND DEATH ACCORDING TO AGE \*

#### MEDIAN SURVIVAL MONTHS



\* 81 DEAD

FIGURE 4

For the over-all series of 100, the median length of survival between the abnormal film and death was seven months for the 39 "suspect neoplasm" cases, 8 5 months for the 26 "tuberculosis" cases, 11 months for the 5 "suspect" cases and 30 months for the 11 erroneous negatives (Figure 5)

Survival According to Clinical Status

The presence or absence of symptoms at the time of discovery was of prognostic importance There were only 10 asymptomatic patients in the series of 100 Four of these lived for more than three years while only one survived three years of the 19 whose symptoms had led them to seek medical advice (Table IX) Had these patients been admitted promptly

TABLE IX  
THREE YEAR SURVIVAL ACCORDING TO CLINICAL STATUS  
AT TIME OF INITIAL PHOTOFLUOROGRAM

Clinical Status	Number	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
"Preclinical"					
Asymptomatic	10	4	40	2	20
Symptomatic	28	7	25	2	7
Clinically Manifest	19	1	5	1	5
Total	57	12	21	5	9

for diagnostic study instead of having been referred for survey films, perhaps their prognosis would have been better When a patient seeks medical advice because of symptoms, he is likely to cooperate in carrying out the advice given

The fate of the "preclinical" symptomatic group was better than that for those with manifest symptoms, 25 per cent having survived three years

Survival According to Bronchoscopic Findings Macroscopic

Bronchoscopic reports were available on 83 of the 100 patients (Table III) For the 64 dead among these 83 patients, the median interval between the abnormal film and death was 8 5 months for the 50 with

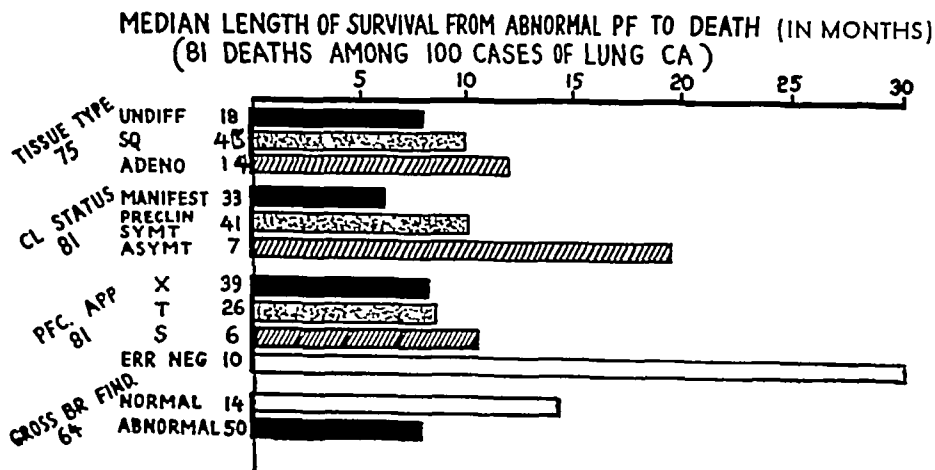


FIGURE 5

abnormal bronchoscopic findings compared to 14 5 months for the 14 with normal findings (Figure 4)

Of the 57 with a minimal follow-up period of three years, 45 had bronchoscopic reports. When any gross abnormality had been visualized, there was only a 19 per cent three-year survival. When no abnormality had been seen, the prognosis was better, 29 per cent having survived. A clearer picture is seen if one considers only the survivors who have been resected (Table X) (Figure 6)

#### *Survival According to Bronchoscopic Findings Microscopic*

Of the 100 cases, there were 21 with positive cytologic reports and 28 with positive bronchoscopic biopsies. Only one survived five years after his abnormal film.

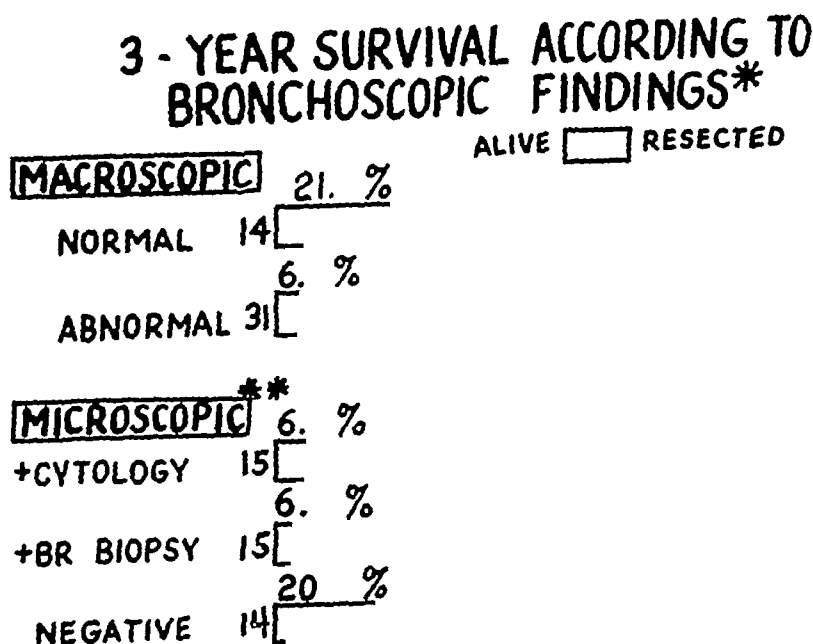
The findings we report are based on a group of patients selected because

TABLE X  
THREE YEAR SURVIVAL ACCORDING TO  
GROSS BRONCHOSCOPIC FINDINGS

	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Not Bronchoscoped	12	2*	17	—	—
Normal	14	4	29	3**	21
Abnormal	31	6	19	2	7
Total	57	12	21	5	9

\*Died within the next two years

\*\*Living and well more than five years after abnormal photofluorograms



\*LIMITED TO 45 OF THE 57 ON WHOM SUITABLE DATA WAS AVAILABLE  
\*\*CATEGORIES NOT MUTUALLY EXCLUSIVE.

FIGURE 6

of photofluorographic abnormality. If we included patients with symptoms but negative roentgenograms and positive bronchoscopic findings, the results might be better.

### *Survival According to Tissue Diagnoses*

The prognosis as in all reported series, was poorest for those with undifferentiated cancers (Table XI). In the series of 100, the median

TABLE XI  
THREE YEAR SURVIVAL ACCORDING TO TISSUE DIAGNOSIS

Tissue Type	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Squamous Cell	35	9	26	4	11
Adenocarcinoma	10	2	20	1	10
Undifferentiated	11	1	9	—	—
Unclassified	1	—	—	—	—
Total	57	12	27	5	9

length of survival corroborates the grave outlook for those with undifferentiated carcinomas. The figures were eight months for the 18 with undifferentiated cancers, 10 months for the 43 with squamous cell carcinomas and 11 months for the 14 with adenocarcinomas (Figure 5).

### *Tuberculosis and Carcinoma*

Ten of the 100 carcinoma patients had concomitant active pulmonary tuberculosis. None survived. It has been repeatedly pointed out that there is a real danger in failing to consider the increasing association of these two diseases in older men<sup>8, 9, 10, 11</sup>. Even when multiple positive sputa confirmed by culture prove the diagnosis of active tuberculosis, radiologic evidence of tumor should indicate exploration in men over 45.

A typical case illustrating the coexistence of these diseases is F B, a 57 year old Negro caretaker who had a photofluorogram on July 26, 1948, read as "moderately advanced tuberculosis of indeterminate activity" because of infiltrations at the left apex and in the right midlung (Figure 7). He was promptly referred to a City Chest Clinic where he was checked and rechecked in an attempt to establish a diagnosis of active tuberculosis. Because his sputum was consistently negative, the survey physician reviewed the clinic film of February 9, 1949 and at once recognized it as suspicious of neoplasm. In retrospect, obstructive emphysema on the right was visible in the film of July 26, 1948. The patient was hospitalized for bronchoscopy. Because the bronchoscopic report did not mention cancer but stated only "bronchoscopy revealed slight medial compression of the right main bronchus just below the carina," the clinic continued to carry the patient as a case of tuberculosis. They obtained a positive sputum October 20, 1948. In January of 1950, the patient was so ill that he went on his own to the Temple University Hospital for admission. Bronchial secretions were positive for tubercle bacilli but, despite this, he was explored February 21, 1950. He was found to be inoperable. Biopsy revealed



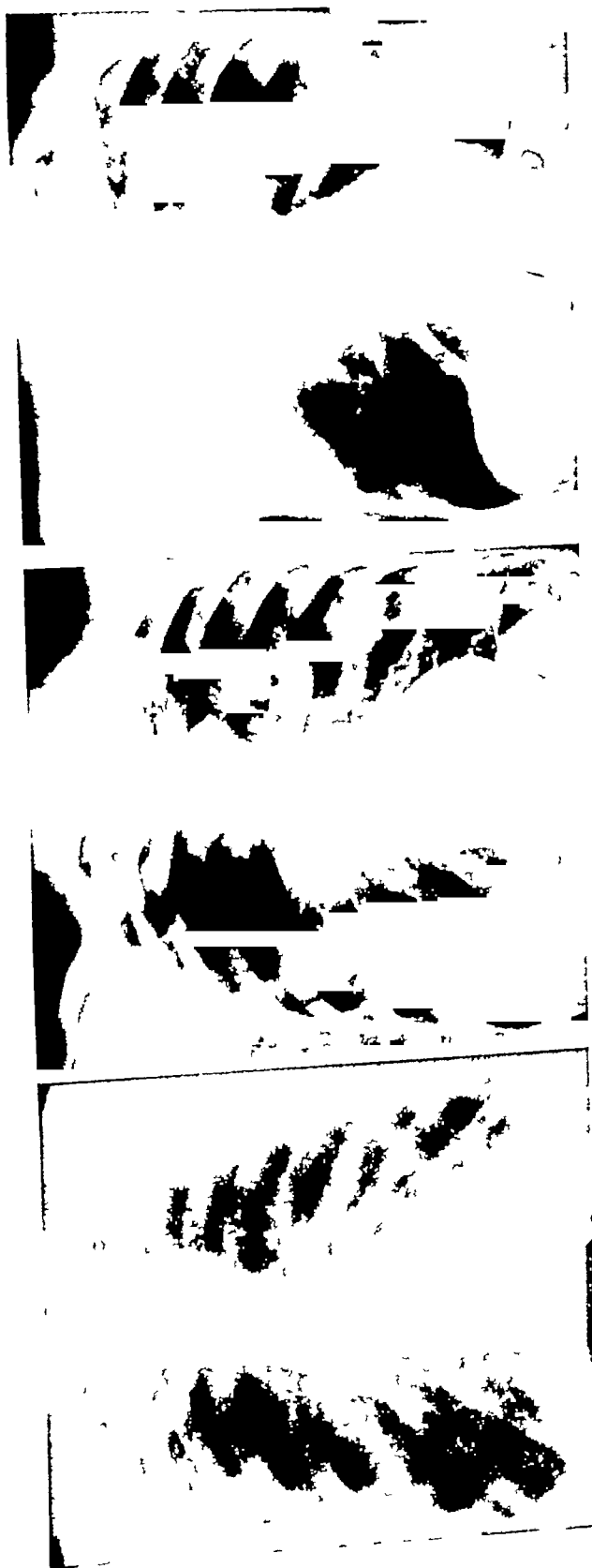


FIGURE 7 F B, 57 N Male Photofluorogram July 26, 1948 read "moderately advanced tuberculosis of indeterminate activity," lesions right mid-lung and left apex (Obstructive emphysema on right missed) February 9, 1949, clinic film reviewed by survey physician because of diagnosis of tuberculosis without positive sputum Patient bronchoscoped but, because only compression was noted, was not explored January 18, 1950, obvious carcinoma Explored, inoperable Repeated positive sputa and biopsy showing squamous cell carcinoma Died December 3, 1950

squamous cell carcinoma Repeated positive sputa grew out on culture The patient died December 3, 1950, having had both active tuberculosis and bronchogenic carcinoma

### *Delay in Hospitalization*

The following data are based on 57 patients with a minimal three-year follow-up period Six men entered the hospital without any delay All died Twenty-three per cent were hospitalized within one month and 33 per cent within three months The mortality experience favored those hospitalized after three months (Table XII)

TABLE XII  
RESECTABILITY AND THREE YEAR SURVIVAL ACCORDING TO  
DELAY IN HOSPITALIZATION

Delay	Number of Cases	Number Resected	Per Cent Resected	Alive Three Years After Initial Abnormal Photofluorogram			
				Total	Per Cent	Resected	Per Cent
None	6	1		1		—	
7 days-1 mo	7	3		—		—	
1 mo -3 mo	6	2		—		—	
Total under 3 mo	19	6	32	1	5	—	—
3 mo -6 mo	5	1		1		1	
6 mo -12 mo	13	4		2		2	
12 mo -24 mo	9	2		2		—	
24 mo -36 mo	7	3		2		1	
36 mo -48 mo	2	—		2		—	
48 mo and over	2	1		2		1	
Total more than 3 mo	38	11	29	11	29	5	13
Over-all Total	57	17	30	12	21	5	9

Two factors may obscure the true relationship between prompt hospitalization and ultimate fate The first is the emergency admission of those whose photofluorograms at once suggest neoplasm and who are mostly already beyond salvage The second is the paradoxical situation in which those whose lesions were inconspicuous have a better prognosis than those whose photofluorograms were recognized promptly as being abnormal<sup>8</sup> One must consider that some whose lesions were missed no doubt developed serious clinical illness or died without returning to the units so that the "erroneous negatives" in our study are probably underestimated and may be selected on the basis of slow tumor growth

At any rate, both the poor prognosis of those with obvious tumor and the better prognosis of those whose lesions were inconspicuous are really facets of the same problem the photofluorographic picture of curable lung cancer has not been delineated At one end of the scale we rush patients into the hospital only to have them die shortly At the other end of the scale we ignore for months or years unimpressive x-ray abnormalities and, even then, we salvage some of them

There is a trend in our series toward increasingly prompt hospitalization. Table XIII reveals that twice as high a percentage was hospitalized within three months among those with less than three years' follow-up as among those with more than three years' follow-up.

TABLE XIII  
DELAY IN HOSPITALIZATION ACCORDING TO LENGTH OF FOLLOW-UP

Delay	Follow-up on those with photofluorograms taken 1-1-47 to 8-31-50		Follow-up on those with photofluorograms taken 8-31-50 to 5-31-53	
	Number	Per Cent	Number	Per Cent
Less than 3 mo	19	33	34	79
3 mo and over	38	67	9	21
Total	57	100	43	100

More rapid hospitalization may well be due to the increased index of suspicion in interpreting films as "suspect neoplasm." Of the 43 patients with less than three years' follow-up, 28 (65 per cent) were classified "suspect neoplasm" while, of the 57 in the group with a minimal three-year follow-up period, only 21 (37 per cent) had been so classified. As time goes on, erroneous negatives may turn up among the recent group. This would shift the percentages.

Individual components of delay were examined for the whole group of 100 (Table XIV). There were three causes of significant delay—the radiologist, the patient, and the clinician.

With such low survival rates, it is fallacious to attempt to weigh the causes of delay according to their importance. Certainly the longest delays

TABLE XIV  
DISTRIBUTION OF COMPONENTS OF DELAY\* ACCORDING TO  
NUMBER OF CASES INVOLVED AND  
MEDIAN LENGTH OF DELAY IN HOSPITALIZATION

Cause**		Number of Cases	Median Delay in Days
Radiologist	Erroneous Negative Report	16	577
	"Suspect" (Inadequate Reading)	5	34
	Inactive Tuberculosis	3	90
		24	367
Administrative Handling of Case		62	5
Patient Delay in Accepting Recommendation		28	141
Clinician Delay in Recommending Hospitalization		52	48
Hospital bed not available at time of application		20	7

\*Based on 91 cases on whom hospitalization was delayed more than seven days

\*\*Categories not mutually exclusive

were due to the missing of lesions. The 16 in this category had a median delay of 577 days. Yet five of these are living, again emphasizing the fact that rate of individual tumor growth is important.

### *Radiological Problems*

Radiological errors were of two types—those in which lesions were missed (16 cases) and those in which lesions had not been classified as “suspect neoplasm” when, on retrospective review, they could have been so classified (25 cases). These are frank errors that can and should be rectified.

There is an additional problem that needs recognition. There are film abnormalities that cannot be considered suggestive of tumor despite the most critical review. We must accept the fact that, just as Newell et al<sup>12</sup> have pointed out their failure to find a reliable classification of the roentgenographic appearance or quality of a tuberculous pulmonary lesion, so we are unable to reliably classify the roentgenographic appearance of curable lung cancer by survey techniques. Once we can accept our limitations, we will recognize the wisdom of considering all photofluorographic abnormalities of the lungs in men over 45 as possibly due to lung cancer. Our highest salvage may well lie in the group whose films least suggest cancer.

The other approach is the follow-up of those with symptoms whose photofluorograms reveal no abnormality. Research in this direction is being conducted through the Philadelphia Pulmonary Neoplasm Research Project<sup>13</sup>.

### *Review of Previous Photofluorograms*

There were 29 patients who had available previous “negative” photofluorograms. On retrospective review, 13 of these remained “negative” but 16 had lesions present which had been missed.

The numbers are small but the fate of the “erroneous negatives” was somewhat better than that of the true negatives (Table XV). Not only was survival a little better but, for those who died, the median length of life was 19 months longer (30 months) for the erroneous negatives than for the true negatives (11 months).

TABLE XV  
RESECTABILITY AND THREE YEAR SURVIVAL ACCORDING TO  
REVIEW OF EARLIER FILMS\*

Review Classification	Number of Cases	Resected		Alive		Resected and Alive	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
True Negative	13	6	46	3	23	2	15
Erroneous Negative	16	5	31	5	31	3	19
Total	29	11	38	8	28	5	17

\* Limited to 29 cases on whom earlier photofluorograms were available.

*Discussion*

A significant amount of lung cancer is being detected by mass surveys. Is such cancer curable? Five-year survival rates are not yet available on significant numbers, but, from the experience of official Philadelphia survey teams, there seems little reason to believe that five-year survival rates of survey-detected cases will be better than the surgeons' depressing figures of under 10 per cent.

We believe these facts should be faced honestly and that every effort should be made to encourage the development of new techniques for earlier casefinding.

A truer evaluation of the possible role of surveys would be obtained if the following principles were adhered to:

- 1 When persistent or unusual respiratory symptoms are present, men over 45 should be referred for diagnostic studies rather than for survey films. One postero-anterior roentgenogram is inadequate even if entirely negative and may well cause false reassurance. Except in a small number of peripherally located cancers, films may continue to appear normal until the occurrence of secondary shadows or gross enlargement of the tumor itself.
- 2 Men over 45 who have no respiratory symptoms should report for photofluorograms every six months. We have had two cases in which patients have been inoperable one year after a negative photofluorogram.
- 3 Survey films should be more carefully read. Unimpressive lesions may be as significant as dramatic lesions, particularly if due to active tuberculosis or cancer. One of the soundest methods for improving the quality of survey readings is meticulous follow-up and routine review by the survey medical team of original photofluorograms when cases of lung cancer are proved. Lung cancer deaths as well as newly diagnosed cases among hospital admissions should be routinely checked against survey files. Comparison of later films with survey photofluorograms brings to light errors and automatically enhances the index of suspicion in the mind of the physician-reader.
- 4 Any abnormality in the chest roentgenogram of a man over 45 should be considered as possible cancer. Since resection offers the only hope for cure at present, physicians should hospitalize promptly all men with such lesions unless there are available serial films and/or histories adequate to diagnose non-malignant disease. At present immediate hospitalization is largely limited to men whose roentgenograms suggest neoplasm.
- 5 Even when active tuberculosis is proved, the possibility of associated cancer should be carefully considered in men over 45. With antimicrobial therapy and present surgical techniques, it is more conservative to resect a tuberculous lesion than to watch a patient who is not responding clinically or who has a shadow atypical for tuberculosis go on to inoperability.

What is the profile of cured survey cancer? There are five resected survivors with a minimal three-year follow-up. Their ages range from 58 to 65, three are white, two Oriental. Three of the five had unimpressive lesions. Four of the five had squamous carcinoma and the fifth had an adenocarcinoma. Four of the five were preclinical in that their symptoms had not been troublesome enough to cause them to seek medical advice. Not one had been hospitalized within three months after his first abnormal photofluorogram. One had not been hospitalized for more than three years.

Apparently, salvage is limited to those with slow-growing tumors. There is a fertile field for investigation of factors related to rate of tumor growth. Age, type of tissue, and hormonal state are some of the factors that may be involved.

### *Acknowledgment*

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### *Summary*

- 1 The prevalence per 100,000 of proved bronchogenic carcinoma among 142,156 surveyed Philadelphians on whom appropriate basic data were available was three for females, 37 for group as a whole, 69 for males, and 284 for males over 45.
- 2 The survivorship of 100 consecutive cases of proved bronchogenic carcinoma detected by photofluorograms taken from January 1, 1947 to May 31, 1953 at two official Philadelphia survey units is presented. Of the 57 patients with a minimal three-year follow-up period, only five (9 per cent) were resected and alive at the end of the three years after their first abnormal photofluorograms.
- 3 Exploration was carried out in 52 instances but resection was only possible in 30. Immediate hospital mortality was 17 per cent.
- 4 Detailed survival studies on the 57 patients surveyed prior to August 31, 1950 suggest a more grave prognosis for those younger than 55, those whose photofluorograms obviously suggested neoplasm or tuberculosis, those with respiratory symptoms severe enough to have caused them to seek medical advice, those with bronchoscopic abnormality of any type, those with undifferentiated carcinomas, and those with concomitant active tuberculosis.
- 5 Paradoxically, the fate of patients hospitalized within three months of their abnormal photofluorograms was worse than that of those with delays of more than three months. Two factors may obscure the true relationship between prompt hospitalization and ultimate fate. The first is the emergency admission of patients whose photofluorograms at once suggested neoplasm and who were mostly already beyond salvage. The second is the better prognosis of those whose film lesions were inconspicuous.
- 6 Examination of individual components of delay in hospitalization

revealed three causes for significant delay—the radiologist, the patient, and the clinician

7. Any photofluorographic abnormality in men over 45 should be considered as possibly due to lung cancer. The highest salvage may well lie in the group whose films least suggest malignancy
8. Of 29 patients on whom earlier "negative" films were available, 13 were still considered negative on review while 16 had lesions which had been missed. The fate of the "erroneous negatives" was better than that of the "true negatives"
9. With present techniques, less than 10 per cent of survey-detected lung cancer appears curable. Suggestions are made for improving the situation currently, but it is recommended that the search continue for new more effective case-finding techniques

#### RESUMEN

1 Entre 142,156 habitantes de Filadelfia en los que se investigó la frecuencia del carcinoma bronquiogénico por cada 100 000—de ellos, y en los que obtuvieron datos adecuados, fué tres entre las mujeres, siendo 37 en el total del grupo, 69 para los hombres y 284 para los hombres de más de 45 años

2 Se presentan los datos sobre la sobrevivida de 100 casos consecutivos de carcinoma bronquiogénico demostrado, descubiertos por fotofluorogramas tomados desde enero 1, 1947 a Mayo 31, 1953 en dos investigaciones oficiales en Filadelfia. De 57 enfermos con un mínimo de seguimiento de tres años, sólo 5 (9 por ciento) fueron resecados y viven al cabo de tres años después de su primer fluorograma anormal

3 La exploración quirúrgica fué llevada a cabo en 52 casos, pero las resecciones fueron posibles sólo en 30. La mortalidad hospitalaria inmediata fué de 17 por ciento

4 Los estudios detallados de la sobrevivida de 57 enfermos antes de Agosto de 1950 sugiere un pronóstico más grave los menores de 55 años. También lo es para aquéllos cuyos fotofluorogramas claramente sugirieron neoplasias o tuberculosis, para aquéllos con síntomas respiratorios bastante severos como para obligarlos a buscar consejo del médico, aquéllos con anormalidades broncoscópicas de cualquier forma, los que tenían carcinomas no diferenciados y los que—concomitantemente padecían tuberculosis

5 Paradójicamente, la suerte de los enfermos hospitalizados—dentro de tres meses a partir de la fotofluorografía anormal, fué peor que la de aquéllos con dilaciones de más de tres meses

Dos factores pueden oscurecer la verdadera relación entre la pronta hospitalización y la suerte final. El primero es la admisión urgente de los enfermos cuyos fotofluorogramas inmediatamente surgieron neoplasias y que ya estaban para entonces más allá de posible—recuperación. El segundo es el mejor pronóstico de aquéllos cuyas—lesiones a la película son poco relevantes

6 El examen de los componentes individuales del retardo en la hospitalización reveló tres causantes de retardo importante, el radiólogo, el enfermo y el clínico.

7 Toda anomalía fotofluorográfica en los hombres de más de 45 años debe considerarse como posiblemente debida al cáncer del pulmón. La más alta proporción de salvaciones bien puede encontrarse en el grupo cuyas películas menos sugieren malignidad.

8 De 29 enfermos en los se obtuvieron películas al principio "negativas" 13 fueron considerados aún negativos al revisarse en tanto que 16 tenían lesiones que habían sido inadvertidas. La suerte de los "negativos por error" fué mejor que la de los "verdaderos negativos".

9 Con las técnicas actuales menos del 10 por ciento de los casos de cáncer descubiertos por la encuesta parece curable. Se hacen sugerencias para mejorar la situación presente pero se recomienda—que se sigan buscando técnicas más efectivas para el descubrimiento de los casos.

#### RESUME

1 D'après une étude portant sur 142 156 personnes de Philadelphie, le taux de cancer bronchique certain fut de

3 pour 100 000 pour les individus du sexe féminin

37 pour 100 000 pour le groupe dans son ensemble

69 pour 100 000 pour les individus de sexe masculin

284 pour 100 000 pour les individus de sexe masculin, âgés de plus de 45 ans

2 Les auteurs rapportent les résultats de 100 cas de cancer bronchique avéré dépistés consécutivement par radiophotographie du 1er janvier 1947 au 31 mai 1953, par deux organismes officiels d'examen systématiques de Philadelphie. 57 malades furent suivis pendant une période au moins égale à trois ans. Parmi eux cinq seulement (9%) furent opérés et étaient encore en vie à la fin de la période de trois ans suivant le jour où fut découverte chez eux une anomalie radiologique.

3 Une intervention exploratrice eut lieu dans 52 cas, mais ce n'est que pour 30 malades que l'exérèse put être réalisée. La mortalité post-opératoire immédiate fut de 17%.

4 Sur les 57 malades suivis avant le 31 août 1950, l'étude détaillée des survivants montre que le pronostic est plus sévère pour ceux qui sont âgés de moins de 55 ans, pour ceux dont les radiophotographies évoquent d'une manière évidente une néoplasie ou une tuberculose, pour ceux qui ont eu des symptômes respiratoires suffisamment sérieux pour qu'ils aillent chercher un avis médical, pour ceux porteurs d'une anomalie bronchoscopique d'un type quelconque, pour ceux porteurs de cancers indifférenciés et pour ceux qui ont une tuberculose active surajoutée.

5 Paradoxalement, l'évolution des malades hospitalisés moins de trois mois après la découverte de leurs anomalies radiologiques, fut plus défavorable que celle des malades hospitalisés dans des délais dépassant trois mois. Deux facteurs peuvent masquer le vrai rapport entre une hospitalisation rapide et l'évolution fatale. Le premier, c'est l'urgence de l'admission des malades dont la radiologie évoque immédiatement une néoplasie, ou qui étaient presque déjà en dehors de toute possibilité d'être sauvés. Le deuxième facteur est le meilleur pronostic de ceux dont les lésions radiologiques étaient incertaines.



6. L'étude des facteurs qui, pour chaque malade, retardèrent l'hospitalisation, révéla trois causes dues au radiologiste, au malade et au praticien

7. Toute anomalie radiologique chez les hommes âgés de plus de 45 ans devait entraîner une suspicion de cancer pulmonaire. La proportion la plus élevée de survie appartient sans doute au groupe dont les films sont le moins évocateurs de malignité.

8. Parmi 29 malades, dont les premiers films étaient considérés comme "négatifs," 13 l'étaient encore lorsqu'un nouvel examen eut lieu, tandis que 16 montraient des lésions d'abord passées inaperçues. L'évolution des "négatifs par erreur" fut meilleure que celle des "vrais négatifs."

9. Avec les procédés actuels, moins de 10% des cancers pulmonaires dépistés à l'examen systématique apparaissent curables. Les auteurs font des suggestions pour améliorer la situation actuelle, mais ils recommandent que des recherches continuent pour découvrir des techniques de dépistage nouvelles et plus efficaces.

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